PRONTOSIL IONIZATION

being

A THESIS for the degree of

M.D.

of the University of Glasgow.

by

James Stewart, M.B., Ch.B.

CONTENTS

INTRODUCTION

INTRODUCTION

An extract from a leading article in the British Medical Journal of 22nd February 1941 is of interest. It said, "Some enterprising clinicians..... had applied sulphanilamide locally with good results, before the work of Fildes and Woods finally gave systemic and local sulphanilamide chemotherapy a completely rational basis ..... Local application is therefore reasonable; whether it succeeds may depend on various local conditions, and can best be decided by practical trial."

The first trial made by me was commenced on 12/4/40 and until June 1940, I was one of the aforementioned group who was unaware that sulphanilamide had been applied locally by others, before the treatments to be detailed herein had been instituted. As reported in the British Medical Journal 6/7/1940. 29. it was an article by J. A. Smith 22/6/40 in the same journal which made me realise that sulphanilamide had been applied locally as a method of treatment by at least eight people, according to Smith's reference.

It was in the latter part of 1939, after observing how quickly tonsillitis was cured when patients first gargled and then drank a mixture containing sulphanilamide,

and the remark made by a drug salesman that sulphanilamide was excreted for the most part unchanged, that the thought occurred that, if this were so, then ionization with sulphanilamide might be effective in treating local streptococcal and staphylococcal lesions. Since it was excreted unchanged, this to me, as a general practitioner, ruled out any chemical change in the stomach and bowel, but indicated that there must be a physical combination of some kind in the body tissues. Should this be the case, then, ran my thoughts, if sulphanilamide could be ionised into the tissues for some little distance around a lesion, this combination with the body fluids would be secured. The necessity of taking it by the mouth, and the toxic effects of which we were at that time warned, and rather timorous of meeting, would be avoided.

Six years ago, I was appointed honorary officer in charge of the Physiotherapy Department of the Royal Lancaster Infirmary. It was the opportunities here offered which made me decide to undertake an investigation on clinical lines to find out:-

1. If Prontosil is suitable to act as an electrolyte

2. If so, is local application of Prontosil effective by ionization in the treatment of lesions contaminated by germs, the growth of which is normally inhibited by, or may reasonably be expected to be susceptible to, the sulphonamide drugs?

3. Which type of lesion is
   a. Especially benefited, and where such treatment should be instituted, with good hopes of success, as the method of election.
   b. Which type is helped in a useful degree in the majority of cases and the treatment rank as one worthy of trial, with fair hopes of success.
   c. Which type is not helped at all, or if so, only on rare occasions, and the treatment only worthy of trial when other methods fail.

4. If the number of cases was too small to formulate any conclusions, could these cases be sifted out, and a pointer gained, giving a direction in which to carry out further investigation.

Later when I learned that sulphanilamide was being applied locally -

5. Is sulphanilamide effective by ionization when local or oral application fail?

An acute infection may heal spontaneously or be cured by simple methods of treatment. It would, therefore, be no useful test of the idea of ionising sulphanilamide, to apply it in any but a chronic and simple case, where no possible harm could result from such an experiment. In March 1940, such a case presented itself at the Physio-therapy Department, a case which was simple (a paronychia), had been in existence for four months, and which the usual methods of treatment had so far failed to cure. This case is reported later and was also mentioned in the article in the B.M.J. 6/7/40. The method was persevered with, and having given hopeful results in a few cases, search was then made into the literature on <u>local</u> treatment with the drug.

Access to the literature has not been easy. Facilities in Lancaster are non-existent and were secured by correspondence with the B.M.A. and other medical libraries - not a very satisfactory method of tracing

references and cross references. With the exception of Otolaryngological journals, which could not be obtained, all reports, so far as can be traced, up to April 1941, on local treatment with the sulphanamide drugs, are included in this essay.

By the time the first case herein reported was treated, about fifteen reports have been traced in British, American, French and German journals as having been published before that date. No reports have been found on ionisation with any of the sulphonamide group of drugs.

Ionization secures a penetration into the tissues much superior to that obtainable by externally applied powder, lotion or ointment. The principle involved in using an electrolyte in ionization which is selective in action against certain germs only, is entirely new. Previously the electrolyte was used as an antiseptic is used - in a general way as distinct from a specific purpose. Dr. A. R. Friel, a pupil of Leduc, and author of several books and articles on ionization, in a personal communication, gave it as his opinion that this new idea may be very important.

The question has been asked, why did I use Prontosil? The sole reason was that in the dispensary there was a large supply in stock which was not being used, having been passed by in favour of preparations not containing dye. Also it was eminently suitable - in aqueous solution, in sterile ampoules, and of a handy concentration. There seems no reason why a British preparation should not be used. Having commenced the investigation with Prontosil it was decided to continue using this drug, and later compare the effectiveness of this one preparation with that of other manufacturers.

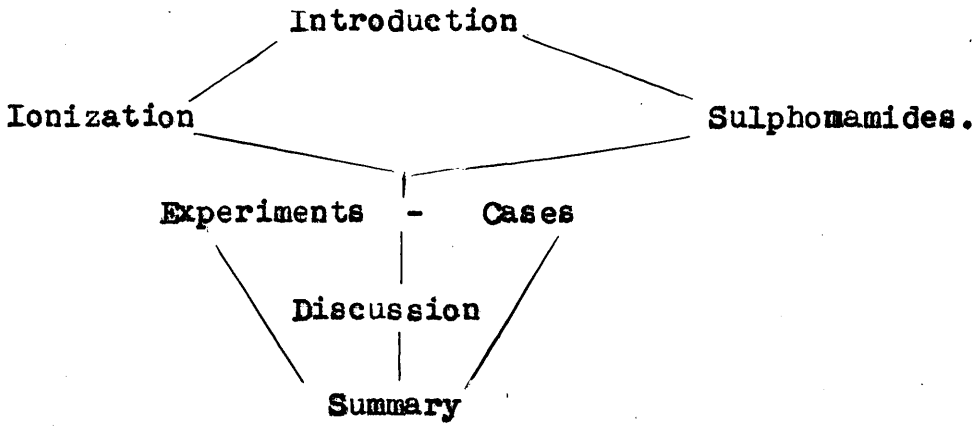
Many others have written to me with the intention of trying this method of treatment. Six months later, after circularising these enquirers, the majority, on account of the war, have been unable to give it a trial, others have not been traced and only one has reported a case. The report from this surgeon is included in the section giving details of the cases treated.

In this thesis, that which follows is arranged after this plan. First a resume of the history, principles, investigations, and results secured by investigators of ionization is given - Next the subject of sulphonamide

drugs is treated on similar lines. The electric and chemical subjects are then combined, first in experiments then as exemplified by actual cases.

The experiments and cases are discussed in a further section and lastly follows a summary.

The plan, therefore, may be illustrated as follows.



References.

I O N I Z A T I O N

IONIZATION

It would be impossible for me to attempt a comprehensive review of what has been written on such a long and well established method of treatment as Ionization. A representative sample of the investigators and of the diseases they treated, sufficient to prove the rationalness and effectiveness of the method, is all that will be attempted in the following notes.

H. Lewis Jones (1) defines Ionization as "a method of treatment whereby electric currents are used to set in motion in a definite direction the constituents of an electrolyte." Friel (2) defines it as "the introduction into the tissues of particles called ions by electric current, and the exchange of ions within the tissues." A combination of the two definitions would probably describe the process more effectively. In brief, it is a means of driving some drug into the tissues of the body by a constant or galvanic current, the basic radicle entering the body under the positive pole and the acid radicle under the negative pole

To apply the principle of ionization to the body, the commonest method is to moisten a pad of lint with the electrolyte and apply this pad (which is just large enough to cover the area to be treated) to the required part of the body. Another pad moistened with a conducting solution, such as sodium chloride, is applied to any other suitable part of the patient. As these pads are fixed to electrodes, the chosen electrolyte undergoes dissociation when the current of a few milleamperes is gradually switched on, and so the desired part of the electrolyte is conducted into the body. This continues as long as the current is running and the longer this is carried out, the deeper into the tissues is the drug driven.

Instead, therefore, of scattering a drug throughout the whole body by oral adminstration to treat one localised area, a purely local action takes place. Drugs can therefore be introduced into local areas to which they could not normally gain access, or, if so, only in extremely minute ineffective dilutions (the sulphonamide drugs are in a category by themselves and this point is discussed later). Wounds can be

treated to a depth not otherwise obtainable, and in greater concentration than the blood could carry to such a site. Toxic action is therefore avoided, a condition always desired, but especially is this so in a weak, debilitated patient or chronic case. The local tissues and the body's defensive mechanism are stimulated. Increased vascularity at the diseased part, concentration of local action and, with Prontosil a bacteriostatic effect, are all gained. Also, there is a break through the attacking ranks of disease and a protective barrier of Prontosil and strengthened, stimulated, defending tissues formed ahead of the attackers, as it were. The ions of a drug are substituted for the ions of the tissues, and become fixed in the tissues. By simple local application, a drug does not become so fixed, but is carried off by the blood and lymph streams. The drinking of well waters, says Luff (3), would not have survived centuries, if not efficacious and is certainly not due to the chemical composition per se, for these can be manufactured chemically. The efficacy of natural minerals depends upon the dissociated ions of the constituents. So too, with ionization as compared

with direct local medication.

The fact that the human body is an electrolyte and that drugs could be introduced through the unbroken skin was, apparently, first recognised by Pirvali, of Venice in 1747. Nearly one hundred years elapsed before similar experiments were carried out by Fabre-Palaprat who attempted medication by ionization with iodine in 1833. Faraday had been investigating the phenomena of electro-chemistry about this time and in January 1834 published the terminology he had devised for describing it. It was then that electrolyte, electrolyze, electrode, cathode, anode, ion etc. were used for the first time.

In a Navy Medical Report from H.M.S. Modeste in 1853 T. Spencer Wells (4), the famous surgeon, gave details of treatments he had carried out as a ship's surgeon since 1847, on ulcers and granulating surfaces using a galvanic current. "The results have been most remarkably beneficial" he quotes. "I have often been astonished at the change effected in twenty-four hours in the condition of ulcers. At one dressing they are seen to be deep, cup-like excavations. At the next

the granulations have nearly reached the surface." Another remark is worthy of being quoted - "I have made numerous trials of the method of Baystow and Scott, of water and dry dressings, of elastic bandages and various other accepted modes of treating ulcers, and have found no means so capable of uniformly producing a rapid growth of healthy granulation as galvanism."

In 1853 also, Hessenstein, and in 1859 Richardson, followed in Fabre-Palaprats footsteps, but unsympathetic criticism, incredulity and marked opposition led to the abandonment of the method. Even Edison (5), renowned investigator as he was, aroused no enthusiasm in 1890 when he published a most interesting report. Not a physician, he was struck by the fact that lithium salts were taken internally to dissolve gouty concretions and secure their excretion. The difficulty of securing the absorption into the system of lithium might perhaps have "more rapid success if the application were made externally, employing the well known principle of electrical endosmose to carry the lithium into the tissues". This method he hoped would bring the lithium more directly into the neighbourhood of the

concretions. After experiments, he used 2% lithium chloride at 4 milleamperes, under the positive pole, for two hours daily, for one week. In the urine 2.43 gms. of uric acid were excreted and 3 ccs. of concretion removed from one finger of an old man of 73 years. The man's general condition was eventually ameliorated and he was able to walk about. (So far I have not tried this method. Cases of gout, in my own practice, have, so far, responded to treatment at home and no other cases have appeared at the Physiotherapy Department.)

From the band of workers, Margaret A. Cleaves (6) must not be omitted. She invented a special speculum to fit tightly against the vulvae and pumped in copper sulphate solution to balloon up the vaginal passage and so secure good contact throughout. By means of the constant current she secured effective treatment in cases of uterine catarrh, gonorrhoea, ovaritis, vaginitis, pruritus vulvae etc. (Pruritus I have treated, and that successfully, but subject to relapses. The same applies to vaginitis but this is now only treated by ionization when Stovarsol

or Devegan short wave or ultra-violet ray treatment fails. Ovaritis I have never treated by ionization nor gonorrhoea)

The foregoing were among the principal prospectors in the field of ionization. They walked a lone trail. The work of Spencer Wells in the surgical field is today held in reverence. His work in physical medicine in the cure of ulcers, and about which he was eulogistic, as the quotation of his actual words shows, is forgotten and unheard of by the great majority.

The sporadic interest in ionization was completely altered at the beginning of the present century by Lewis Jones in this country, and Stephane Leduc in France. They placed it upon a sound scientific basis, and firmly established ionization as an established method in the treatment of many diseases. The absorption of drugs by electrolysis was believed to be insignificant, and due to skin absorption only. Leduc (7) applied a pad moistened with strychnine sulphate to a rabbit without affecting it at all, even when left indefinitely. When the galvanic current was applied, however, the rabbit dropped dead. Iodine can be found in saliva and

urine about a quarter of an hour after ionization with that substance. Apart from convincing the world that ions entered the body in an appreciable degree, much important work in the experimental and practical fields was carried out by these two outstanding men - the velocity of penetration, depth of penetration, quantity deposited, the methods of application of drugs, the diseases benefited, the poles to use, strength of current, duration of treatment, in brief the pharmacopoeia, as it were of ionization. Successful results were obtained by Leduc (7) in the treatment of ankylosed joints, glands, abscesses, neuralgia, warts, fibrositis, alopecia etc. (Since Leduc's time the armamentarium of the physiotherapist has been greatly implemented with very more efficient machines. Thus for ankylosed joints I have found short-wave or infra-red ray treatment more effective in some cases than ionization. For adenitis, ionization is rarely used, ultra violet ray treatment being most efficacious and is almost specific. Abscesses did respond to zinc ionization, but Prontosil, in my opinion replaces zinc as the electrolyte of choice and that, in a very

decided manner. Neuralgias respond to ionization but equally good results are obtained now from infra-red ray and sometimes short-wave therapy, as does fibrositis. Ionization is still useful in wart eradication).

Jones (8) covered the same field as Leduc but had happy results in the treatment of rodent ulcers with zinc, and was interested in experiments on lupus. Until combined with radium therapy, by Doyle (9), rodent ulcers recurred within six months in 25% of cases, permanent cure was attained in all cases by the combined method. (I have never treated a rodent ulcer.)

Friel A.R. (10) specialised in the treatment of ears and noses with outstanding success. (Ears, I have found difficult to cure with zinc ionization. They either were cured in three or four treatments or not at all, more often, not. Prontosil ionization is somewhat more effective in otitis media. Zinc ionization in Hay Fever is very effective but Prontosil is better than zinc in nasal catarrh treatment).

A case of colitis sent to him by Arthbuthnot Lane was cured by Webb (11), who ionised the colon with 0.1% silver nitrate, thus gaining the absorption of the

silver into the protoplasm of the cells.

Tayler, H.P. (12) had good results in cases of rodent ulcers, lupus, diphtheria and neuritis. (Lupus has always been treated by me with ultra-violet ray treatment, the Kromayar lamp being especially effective. I have had no failures with a fairly large number of cases although treatment has had to be prolonged. The results have been aesthetically so good, I have seen no reason to change in view of the reports of other treatments. Only one case of diphtheria has been treated by me and that was experimentally cured with Prontosil. Normally Diphtheria cases are better kept outside a general hospital.)

Finzi, N.S. (13) cured many cases of chronic varicose and syphilitic ulcers with zinc. (Syphilitic ulcers I have never treated but with varicose ulcers I have had good results with zinc as with Prontosil ionization).

Bokenham, T.J. (14) reported 21 cases of haemorrhoids cured after only a few treatments by zinc ionization (I have not been so successful. Results have varied).

For three years Riddell (15) had no failures in the treatment of fifty-three cases of ringworm, using a 1% solution of mercuric chloride, or 1% watery solution of iodine.

Taylor and MacKenna (16) cured lupus, when X-ray and ultra-violet ray treatment failed. They improved on ordinary zinc ionization, by briskly rubbing the ill-developed epithelium with liquor potassae, and then applying the usual ionization treatment with zinc. This method allowed treatment of active foci in the depths, and gave a much superior scar.

Most of the diseases benefited by ionization have been mentioned above. The reports quoted, however, are only representative of a vast number in the literature. The names selected have been those who have first investigated a particular disease, or developed a new method in treatment. Sufficient data has been mentioned to prove the efficacy of ionization. Further quotations would seem to be redundant, for Ionization will be used daily in every hospital possessing a physio-therapy department. As L.D. Bailey (17) most succintly says "A few pioneers have not only attempted but have succeeded in placing this science on a reputable basis, if not on a secure foundation. That the foundation is insecure is not the fault of the pioneers themselves, but due to the fact that the peoples of the countries which they have invaded (if such a term is

applicable) have been slow to appreciate the benefits of the methods with which, until recently, they have been unacquainted, though the majority make use of them."Timeo Danaos et dona ferentes."

CHEMOTHERAPY.

CHEMOTHERAPY

Sulphanilamide was first mentioned in 1908 by Gelmo (18) a German chemist studying azo dyes. Eisenberg (19) five years later, suggested the use of sulphanilamide in Medicine, when he discovered the bactericdal powers it possessed in vitro. Two other German chemists, Mietsch and Klarer (20) synthesized sulphonamide -chrysodine, patented it, calling it "Prontosil." Domagk (21) working with the two last named chemists, discovered the specific power of Prontosil to overcome streptococcal septicaemia in mice.

Becker (22), affirms Bayer, was the first to use Prontosil as an external application. He used it in a variety of cases, carbuncles, abscesses, traumatic ulceration and in skin diseases, claiming good results.

Purdie and Fry (23) in the same year, 1937, were the first in this country to apply sulphamilamide locally to a wound. This was a chronic wound infected by streptococcus haemolyticus following puerperal sepsis three years previously. By administering p-aminobenzene-sulphonamide orally and irrigating the wound with a 1%

solution of the drug, the wounds were sterilised in three weeks, and complete healing resulted in six. Various operative procedures and ultra-violet ray treatment had failed to give any relief. They believed the result was not a spontaneous cure but to be due to the sulphanilamide powder in solution.

About the same time, it was suggested by Sigel (24) that Prontosil might be useful as a prophylactic in the treatment of infected, or dirty wounds, and obtained primary healing when he gave it from the start in some heavily contaminated cases.

Jaeger (25) cured certain skin diseases using Prontosil locally, and Tiling (26) treated cases of streptococcal empyema with intra-pleural injections of the same drug.

Colebrook and Kenny (27) injected Prontosil into the peritoneum of mice and four days later, a culture of streptococci. There was no toxic effect, and out of twelve animals so treated, two died within three days. In untreated controls, however, nine died.

According to Buttle, Gray and Stephenson (28) when testing variations of sulphonamide, the drug was active

against streptococci, gave some protection against meningococci, but not against staphylococci, or pneumococci. Jensen (35) and Milian (63), to mention but two names, found that sulphanilamide was effective against staphylococci. (In my experiments Prontosil did on every occasion inhibit the growth of staphylococcus aureus and five cases out of six were cured when staphylococci alone were found and the sixth was greatly improved. Many cases of mixed infection - streptococci, staphylococci and pneumococci - reacted favourably and were cured. Sulphanilamide therefore, in my opinion, does inhibit these germs. In my series no meningococcal cases were met).

Good results against streptococci, both in experiments on mice and again in man, were reported by Long and Bliss (29)

Sinclair (30), a Canadian dentist, tried the effect of sulphanilamide locally in root sockets of infected teeth and in compound fractures of the jaw, securing more prompt healing as a result.

An ointment containing Prontosil and applied locally in furunculosis and impetigo cleared these conditions

up - Merz (31).

In 1937, Bohlman (32) suggested oral administration for crushing injuries and compound fractures, and later tried local applications with success. He cites Mellon and Co-Workers (33) as reporting that sulphanilamide does not neutralize toxins, but that it increases the mobilizations of phagocytic cells at the site of infection, and has a bacteriostatic effect. (With regard to the statement that sulphanilamide does not neutralize toxins, my patients, after treatment, consistently stated they felt much better the following day. This could not have been entirely due to the cleansing of the wound and consequent reduction in absorption of toxins. It was too rapid. It may have been psychological to some extent, but this would not occur in every case. Case 35 (See Case Reports) died of toxaemia, after treatment was stopped, but his toxic condition improved so much with prontosil ionization that it was visible, even to his relatives. Oral administration may not, visibly nor objectively, appear to neutralize toxins on account of its own depressing effect, but by ionization, I am of opinion that it does, to some extent, neutralize toxins. The report of my experiments show the bacteriostatic

effect to be most definite and powerful)

Since writing this, the paper by Osgood and Brownlee (34) has been perused. In this paper it is stated that the major action of sulphanilamide on the haemolytic streptococcus seems to be neutralization of the toxins. It decreases the rate of cell division, and does not kill these organisms directly. It allows the bactericidal properties of the human serum and phagocytosis of leucocytes to kill the germs. There is no direct effect on phagocytosis, they believe. A case is quoted by Mellon, in which cultures revealed a pure growth of streptococcus haemolyticus, but after treatment yielded a growth of diphtheroids and comment is made on the reversibility of dipheroids to streptococci (Did this occur in Case No. 12 herein reported?)

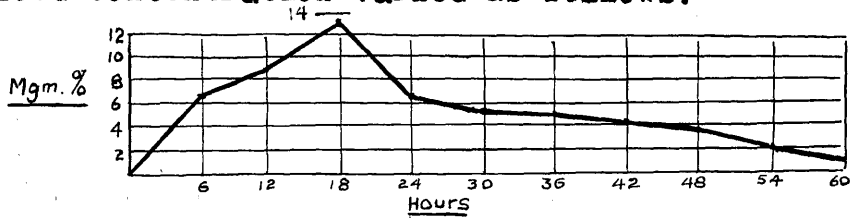
The interest in sulphanilamide and the research taking place from 1938 onwards, may be likened to a spearhead - broadening widely, the further we go from the point of attack. It becomes increasingly difficult to place each worker in chronological order according to his due, and at the same time not be left with a jumble of chemistry and practical experiments. As the paper

deals with local application, the research dealing with oral administration of the drug has been omitted, except so far as it may affect local lesions via the general systemic route.

In "Recent Advances in Chemotherapy" (1939), Findlay (35) states that sulphanilamide, when given orally or subcutaneously, becomes widely and uniformly distributed in the body, except in bone and fat, which have a smaller concentration, and less in the plasma, than in whole blood. It is found in saliva, sweat, bile, pancreatic juice, plasma etc. It passes too, into the amniotic fluid and the foetus, when given to pregnant rabbits. In man, it passes slowly into the cerebro-spinal fluid. (Experiments 4 and 10 with Prontosil gave a visible confirmation of the widespread distribution after ionization, but this is fully reported on later in the list of experiments carried out by me.)

Given by mouth or intramuscularly, a concentration of 10 - 20 mgm per cent in the blood may be secured. A single dose reaches its maximum concentration in the blood in a few hours and is soon being excreted. The maximum concentration, however, can be maintained by

smaller continued oral administrations. Here, however, the danger of toxic symptoms looms up, so that where possible external application would be the ideal, especially so, in weak or debilitated patients. Again, by local application, the wounds can be saturated with sulphanilamide. A concentration, around the wound, approaching 800 mgm. per cent for some considerable time is secured as against the 10-20 mgm. per cent obtained by systemic medication.- Jensen, Johnsrud and Nelson (36). Stuck, Maxwell and Monsalvo (37) quote similar figures. Jensen after implanting 10 gms. of sulphanilamide in a wound, found the blood concentration varied as follows:-



On the other hand, the concentration in the serum of the wound itself is shown in this interesting table

Amount placed in wound	Hours since closure	Local concentration in mgm. %	Blood concentration in mgm.%
5 gm.	24 hours	666.5	2.7
10 "	26 "	509.0	-
8 "	30 "	250	5.9

Most antiseptics are used in concentrations which destroy the leucocytes before destroying the bacteria - Fleming (38). Sulphanilamide, he states, only affects leucocytic function in concentration some twenty-five times greater than can be attained in the human body, while it inhibits the growth of streptococcus pyogenes in concentration one-fiftieth of such therapeutic contentration. He summarised its properties as follows:-

1. Sulphanilamide is specific in action.
   (With four exceptions, all the cases treated in my investigation were types known to be susceptible to sulphanilamide. No comment can therefore, be made on this point)
2. Sulphanilamide has little antibacterial action when large numbers of bacteria are present.
   (This is definitely so in many of the cases reported which failed to react to ionization, especially those with ear troubles. Mention is made of this in the discussion later).
3. Sulphanilamide is inhibited in action in extracts of bacteria and in peptone.

4. Sulphanilamide is essentially bacteriostatic in action and the defences of the body complete the destruction of the bacteria.

(All my cases confirmed this point as did my experiments 6, 7, 8, & 9, so far as the action of Prontosil Ionization is bacteriostatic).

On another occasion, Fleming (39) showed that serum and sulphanilamide inhibits the growth of streptococci, but blood and sulphanilamide did not do so. Local application should therefore on this account be more effective. Against this is the fact that in contact with pus, with a large number of bacteria, or with peptone, the action of sulphanilamide was hindered, or no action at all took place. Theoretically, states Prof. Fleming ".....sulphanilamide should not be a very good antiseptic for wounds that are really septic." "It might, however, be argued that it would be quite easy to wash out the pus from the cavity of the wound, and that sulphanilamide then applied locally would succeed. We have now to consider the sloughs which cannot be washed away. These, like the pus, contain multitudes of bacteria and many broken down cells which, in their breaking down, have liberated proteolytic ferments, and these in their turn have broken down

proteins into peptones. The position in the sloughs is, then, exactly as it was in the pus and there could be no reasonable hope of local application of sulphanilamide influencing the infection." (It is most definitely true that sulphanilamide is not effective in the presence of much pus. This is exemplified in some of the cases of otitis media etc., where the cleansing by H_2O_2 was not satisfactory. On the other hand, patients have been cured where sloughs were present. My opinion is that this was effected by the Prontosil being forced in behind the slough by the current, as a pincer movement. Local application of a powder had proved to be useless. The success, or otherwise, of the ionization method depends on the slough not being too "juicy" and on the cleansed part of the wound being freed from liquid pus after treatment, and also to a good blood supply to the part. When once this foothold has been gained, the pincer movement by ionization is extended by each subsequent treatment).

Buttle (40) found that against bacteria in a poor medium for supporting growth, e.g. urine or blood, systemic treatment by sulphanilamide is very effective, but, if in a good medium e.g. a collection of pus or other

products of tissue break down, drugs have little effect. Sulphanilamide should be more effective in prophylaxis than in cure. Locally sulphanilamide has not yet been used extensively.

In the experimental field Jensen (36) fractured ribs in mice and contaminated the fractures with staphylococcus aureus. The result of treatment was - incidence of infection in controls 71%, when sulphanilamide was given systemically 80%, and when given locally only 20% A few months after the publication of this paper Nitti (41) presented his report on local application of sulphanilamide to artificially produced wounds. There was no sign of local irritation in doses of 1 - 2 gms. per kilo and even up to 5 - 6 gms per kilo, little toxicity was shown. The effect was much more prolonged than by the mouth, though the concentration in the blood itself was not so great. The animals, artificially wounded, the wounds infected with streptococci, then packed with sulphanilamide, survived for 8 - 10 days, if not indefinitely. He envisaged with confidence, the preventative and curative treatment of septic complications of war wounds, and of local treatment as a precious adjunct to oral administrations.

At the Pasteur Institute, Legroux (42) reproduced a condition equivalent in microbic state to a war wound of 12 - 30 hours duration, by crushing the Adductor Magnus Muscle in guinea-pigs, implanting a small square of cloth infected with a culture of streptococci and then suturing up the wound. The animals died in 18 - 48 hours. When however, sulphanilamide was placed in the wound as well, death was delayed three days and for a further three days if the wound was opened and more powder insufflated. If, instead of this insufflation, sulphanilamide was now given per os, life was prolonged for twelve days, and by removing the fragment of cloth and pus on the twelfth day and repulverising, the animal lived indefinitely. Infection once established was not stopped by the insufflation of the wound, nor by oral treatment. These experimental findings were confirmed in the French Army, when it was found that to have sulphanilamide in wounds immediately was much more effective than to wait for debridement. (I have given none of my cases sulphanilamide by the mouth. To have done so would only have introduced doubt as to which treatment was giving result. Again, Legroux states, that when infection was established, insufflation of the wound

or oral treatment by sulphanilamide did not effect the wound. This is true of several of the cases reported later, but the infection was overcome by ionization, even when it had been established for some considerable time).

Experimenting on rabbits' brains with local application of sulphanilamide, Russell and Falconer (43) found no appreciable damage to the tissues but excessive quantities gave rise to foreign body reaction.

In experiments carried out by Hawking (44) on guinea-pigs, local treatment was more effective in preventing infection of wounds by gas gangrene organisms than systemic treatment. The untreated animals died in twenty-four hours. Treated animals, for the most part, were saved.

Reports of actual local treatments of human lesions are fairly numerous and show great diversity of diseases treated, although the numbers of cases quoted are not large.

Glover (45) successfully treated Gonococcal Ophthalmia Neonatorum.

In the treatment of boils, carbuncles, cellulitis, infected wounds, abscess cavities, varicose ulcers, burns and tonsillitis, Bosse and Bosse and Schirp (46)

employed sulphanilamide in lotion, powder and ointment. Some cases, which responded poorly to oral treatment, were cured by local application. (With the exception of tonsillitis, similar types of cases, which failed to react to oral or local treatment are quoted in this thesis and were cured by the ionization method.)

Chandler (47) had good result in the treatment of chronic osteo-myelitis.

Sezary (48) reports excellent results by using powdered sulphanilamide locally in the treatment of soft chancre and in skin lesions, and quotes Hanchell and Lepinay as having had like cures. Gate and Cuilleret, he states, found powdered sulphanilamide per se was more efficacious than when used in the form of an ointment. (In dermatitis, I found Prontosil ionization did not prove of any use. The germs were controlled, but the skin was not stimulated to new growth. It was effective in furunculosis, boils and impetigo contagiosa.).

In an outstanding report Jensen, Johnsrud and Nelson (36) gave details of a method they evolved by inserting 5 - 15 grms. of sulphanilamide, after cleaning up the wound, into compound fractures and compound dislocations. Forty-one

cases were treated and all healed by first intention except two, which were re-compounded and later healed perfectly. Their rate of infection had previously been 27%. This paper, after its publication in July 1939, apparently aroused the interest of surgeons in the use of sulphanilamide. In the following year many reports appeared.

Brittain and Latter (49) and Hodgson and McKee (50) found that wounds treated after the manner of Jensen, showed beneficial results, post-operative infection and pyrexia were exceptional and that even Cl. Welchii infection remained confined to the wound.

Levaditi, Gerrard-Moissonnier, Brechot and Tournay (51) secured very satisfactory results in the local treatment of twelve old wounds. All markedly improved.

The curative properties of sulphanilamide against human infection by haemolytic streptococci, and by some of the gas gangrene organisms, state Fuller and James (52), make this drug of great importance in the treatment of war wounds. Most deaths from infections in the Great War were due to these two groups of organisms. The haemolytic streptococci were also responsible for the

great majority of complications (Douglas, Fleming and Colebrook, 1920)

90% primary healing in compound fractures was secured after locally implanting sulphanilamide by Watson Jones (53). Nor, he states, can there be any doubt as to the value of these preparations (sulphanilamide) in such cases.

Dealing with drunks and patients in poor physical condition, Stuck, Maxwell and Monsalvo (37) treated twenty-one fresh compound fractures and five compound fractures which had previously had osteo-myelitis of some months duration. These cases were all plated and closed without drains. Twenty-two healed by primary union, the others, at the time of the report had not then healed.

The War Office (54) recommended the implantation of sulphanilamide into the depths of wounds at the time of debridement. Owing to the outcome of the campaign in France, and the chaotic conditions prevailing, few cases of local treatment were able to be followed up and reported on - Page (55). His impression was, that the incidence of secondary infection in wounds treated with sulphanilamide was lower than he expected from his experience of the last War. Colebrook (56) spoke in much the same strain and

quoted one series of seven or eight cases. Two had acquired a streptococcal infection; the others healed by first intention. At two C.C.S. ten cases treated by packs remained free from infection up to five days after treatment. Handley (57), Ogilvie (58), Page (59) and King (60) all reported their impressions as being favourable in the war wounded they had treated. Ogilvie based his opinion on three hundred cases from Dunkirk. King was the first to quote actual cases and these were from memory. He cleansed the wounds with Peroxide after surgical treatment, and then packed with sulphanilamide. No such cases died, and even wounds 48 - 72 hours old showed improvement in their condition. When the powder ran short, and flavine packs were employed, some patients died and most had toxaemia in some degree. (It is of interest that in February, 1941, King should remark the beneficial effect of H_2O_2 combined with sulphanilamide. This has been the routine treatment given in my cases since April 1940)

Riches (61) and Buxton (62) treated air raid casualties with powdered sulphanilamide and found the method satisfactory.

In Sir Harold Gillies' plastic surgery unit, Colebrook (63) eliminated infection from superficial granulating wounds. He had been astonished at the results in old burns and infected road accident cases.

In acute infections of streptococci and staphylococci such as impetigo, Milian (64) found an alcoholic solution of sulphanilamide effective as a local application.

Septic sinuses cleared up after irrigation with Prontosil soluble - Childrey (65).

By injecting Prontosil into the pleural cavity, Smith (66) cured an empyema in a remarkably short course of treatments. Other cases which responded well were abscesses, where gauze soaked with the sulphanilamide preparation was used as a packing, or by the use of an ointment.

Two nurses having been found to be nasal carriers of diphtheria, Payne and Auchinleck (67) instituted frequent use of a sulphathiozole snuff. The swabs were negative on the second day and remained so for 7 - 12 days. (Case No. 12 was a nasal diphtheria which was cured by ionization with Prontosil. It is only suggested that ionization might prove of use in refractory cases of nasal diphtheria.)

In the post-operative treatment of resection of the rectum, Mayo and Miller (68) after cleansing with Hydrogen Peroxide, used irrigations of sulphanilamide in normal saline. A year's work on these lines had proved very satisfactory. They believed that this use of peroxide of hydrogen had enhanced the action of the sulphanilamide in accordance with Shaffer's theory that the mode of action of sulphanilamide is due to its oxidation products. (I have previously mentioned the routine treatment adopted in my cases. I have been hoping to meet a patient with two fairly similar lesions to treat one lesion with H_2O_2 and then apply Prontosil and the other diseased part treat with H_2O_2 and ionise with Prontosil. No such case has yet appeared. This particular control is at present lacking. It must be noted that a good number of my cases had been treated locally with sulphanilamide powder and then cured with ionization).

At the Mayo Clinic, Herrell and Brown (69) using a solution of sulphanilamide in normal saline, treated twenty-one cases of operative and traumatic wounds of the scalp, thorax and pericardium as well as fractures and sinuses. The results, though not uniform, were so

satisfactory as to justify continuation. They believed the beneficial effect of local application can be explained to some extent by absorption. On the other hand the absorption, where the wound area was small, was so slight as to be indetectable. The results were out of proportion to the response expected from the concentration present, judged by other methods of administration. (This may be explained by the amount of serum present. I have noticed with ionization, that after several treatments a wound tends to become tanned by the Prontosil. It becomes dry. The astonishingly rapid growth of skin or healing tissue now slows down at this stage. The ions of the tissues have been replaced entirely by Prontosil ions. The concentration can be too great. The body fluids can not then play their important part)

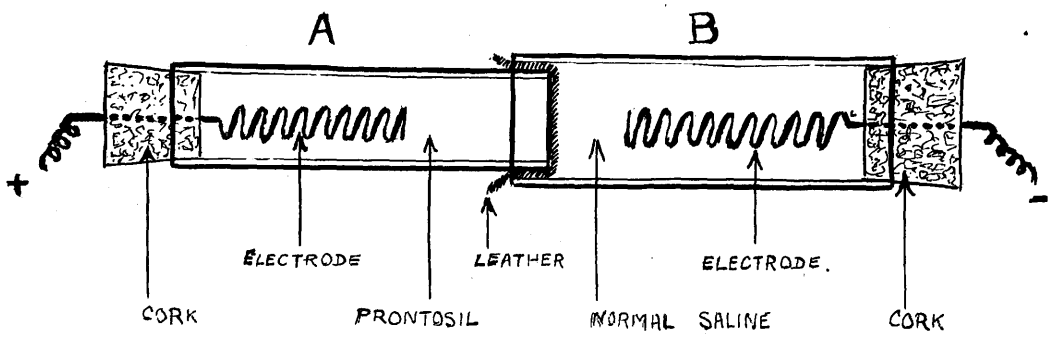
Unusual ill-effects were reported by Frankland (70) and Fletcher (71). The former quoted six cases of foot-drop, gluteal paresis and ulceration of the skin with persistent sinus, following injections of sulphanilamide. Fletcher quoted a case of complete anuria with fatal termination following sulphapyridine treatment by the mouth in a case of pneumonia. The more common

toxic effects of oral administration need not be discussed at length - nausea, vomiting, abdominal pain, diarrhoea, anorexia, malaise, weakness, vertigo, tingling, disorientation, rashes, acidosis, cyanosis, hyperpyrexia, shock, jaundice, sulphaemoglobinaemia, anaemia, leucopenia, agranulocytosis, optic neuritis and psychosis - Bigier and Haralambie (72)

These complications, if uncommon, are nevertheless entirely avoided when local treatment is utilised. For local lesions, local treatment is, according to the reports previously quoted in this section, of undoubted and inestimable value. As a local prophylactic the sulphonamides are almost a definite guarantee of a smooth, uncomplicated, healing by first intention. When infection has taken place, local treatment is not so unfailing but nevertheless is of paramount importance.

EXPERIMENTS

EXPERIMENT No. 1.



A glass tube (A) was plugged at one end with a cork through which passed a wire electrode, as indicated. The other end was covered with fine leather. This tube was filled with 5% Prontosil Soluble. The leather covered end was jammed tightly into a slightly larger tube (B), filled with normal saline and plugged at the other end by a cork through which was fitted a coiled wire electrode.

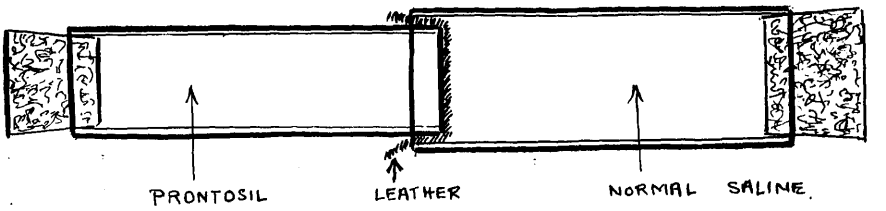
A galvanic current of 5 mille-amperes (5 M.A.) was passed, the positive terminal being at the Prontosil end of the combined tube, and the negative at the normal saline end.

In five minutes a faint ring of colour around the edge of the leather drum was observed to have come through into tube (B). In 10 minutes the drum was covered with dye,

and in another five minutes the surface was densely stained and diffusion into the normal saline itself had taken place for about 1/16th inch in depth. The tubes were separated and the parchment shaken free of superfluous fluid. After washing the glass tubes, the parchment was replaced and equal quantities of clean water placed in each. The tube was shaken to wash the leather on both sides. The solution on the Prontosil side (A) was somewhat darker than that on side (B).

CONCLUSIONS. When a galvanic current is passed through Prontosil soluble under the positive pole, passage of the red dye at least takes place through a leather membrance. The amount passed is quite appreciable and takes place rapidly.

EXPERIMENT No. 2.



The same tubes were used as in Experiment No. 1, but without the electrodes, and without the passage of any current. Osmosis alone was allowed to take place.

In five hours a very faint staining could be seen on the normal saline side of the leather and it took twelve hours before the coating was as dense as it had been after fifteen minutes of ionization.

CONCLUSIONS. Comparing experiments 1 and 2 the passage of Prontosil through a membrane by ionization is about fifty times as rapid as by simple osmosis.

EXPERIMENT No.3.

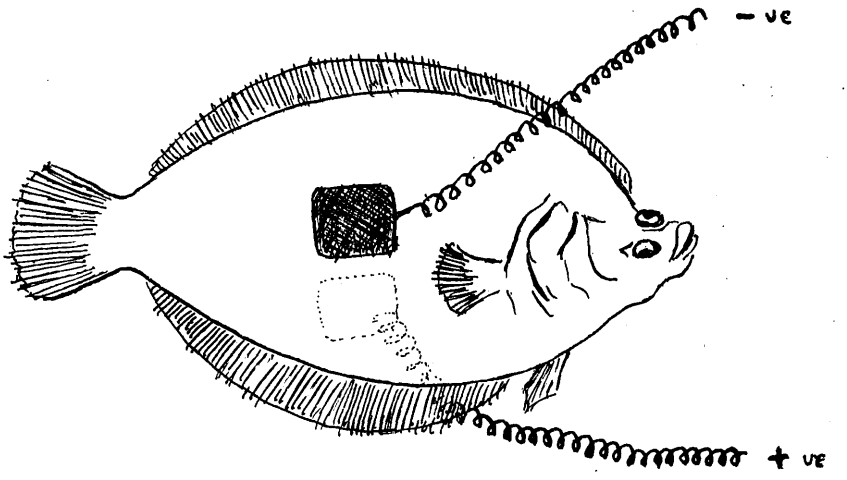
Using the same tubes as in Experiment 1., the Prontosil tube (A) was connected with the negative pole and the galvanic current passed at 5 M.A. for 15 minutes.

No staining was visible on the membrane, and the same conditions prevailed for a further five minutes at double the amperage.

When the current was reversed, staining was visible in five minutes.

CONCLUSION. Prontosil is only ionisable under the positive pole.

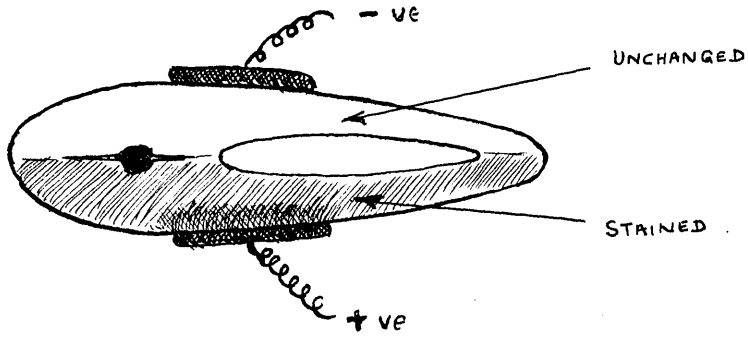
EXPERIMENT No. 4.



On the upper side of a live flounder an electrode was placed as indicated. This pad was soaked in normal saline and attached to the cathode. The positive pole, the pad of which was moistened with Prontosil Soluble was placed on the under surface. A current of 10 M.A. was passed for five minutes.

In two minutes the fins and tail showed pink. The fish, alive at the end of the five minutes ionization was killed, after being well washed. The skin was deeply stained at the site of the Prontosil pad. Scraping

showed that the dye had penetrated the skin. When cut open, the flesh of the under half of the fish was stained a pale salmon pink up to the vertebral column. The upper half of the fish was unchanged. There was greater concentration towards the site of the active pole.



CONCLUSIONS In the living fish, Prontosil is rapidly driven through the skin by ionization into the tissues and blood stream, for the fins and tail became tinged within 2 minutes. Within 5 minutes the Prontosil had entered and become fixed in the living muscle tissues extensively and to the depth of half the fish ($\frac{3}{8}$"). The circulatory system was insufficient to carry all the Prontosil away as it pierced the skin. It had passed direct into the muscle.

EXPERIMENT No. 5.

A pad, moistened with Prontosil, was applied to a live flounder for 15 minutes. The fish was well washed and then killed. The washing removed a considerable amount of the deep staining originally present, the skin being faint pink in colour only. Scraping removed the last traces. The muscle tissues were not affected at all.

CONCLUSION - Local application of Prontosil does not penetrate deeply, nor does it become fixed in the cellular tissues when applied for a period three times as long as in the (previous) ionization experiment.

EXPERIMENT No. 6.

The following experiments are based on those carried out by Prof. Fleming (Proc. Royal Soc. Med. Jan. 1940. 9.127).

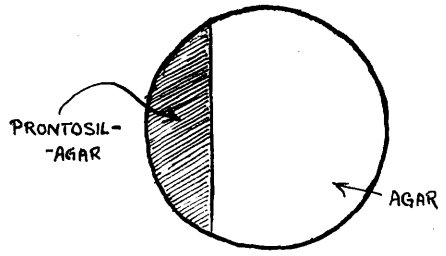


FIG. 1.

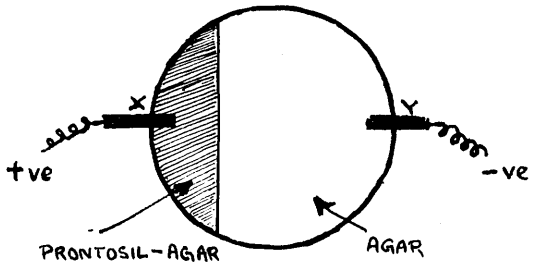


FIG. 2.

A Petrie plate had a segment of agar removed. This space was replaced by agar containing 1% of a standard 2½% Prontosil solution (i.e. 0.025% actual Prontosil content). FIG. 1.

A similar plate was prepared having thin tin electrodes implanted at X and Y as indicated in the above diagram. FIG 2. X was the anode and Y the cathode respectively. The tin electrodes were bent under the cover of the Petrie plate and embedded in the culture medium as shown. FIG. 3.

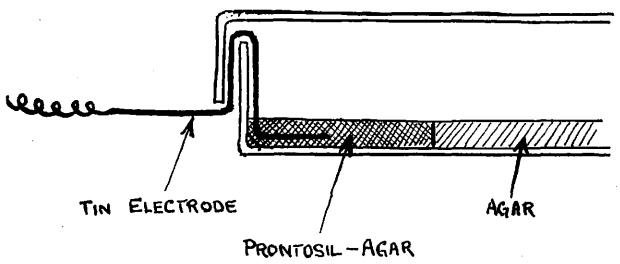


FIG. 3.

A broth containing Staphylococcus Aureus was made, and also two dilutions, 1 in 10 and 1 in 100. Loopfuls of these were drawn across the two plates, the strokes commencing the same distance CC from the junction of Prontosil-Agar and Agar LD (hereinafter called the line of demarcation). FIG. 4.

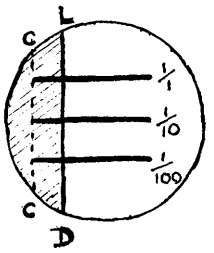


FIG. 4.

The plate with the terminals was subjected to a Galvanic current of 10 M.A. for five minutes. Both plates were then placed in an incubator and observed after twelve and twenty-four hours.

RESULTS Many experiments were carried out. The results were all similar, differing only in degree. The growth depended on the strength of the broth, the only variable. Diagramatically the growth is represented hereunder. The measurements and character of the number of colonies are taken from an actual average culture.

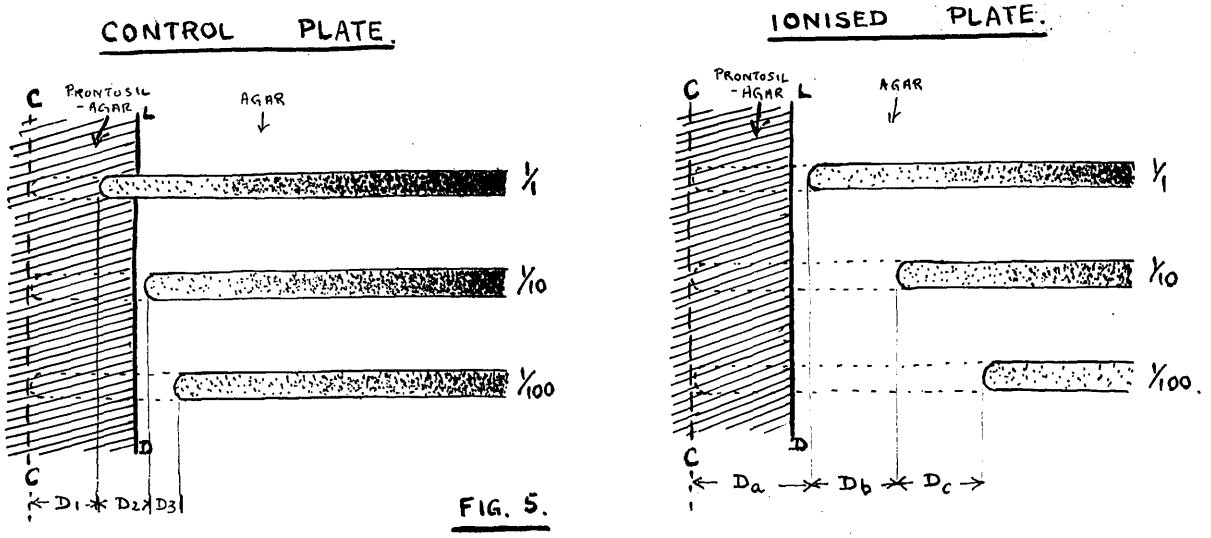


FIG. 5.

In neither plate did growth grow to CC. The stronger the broth, the nearer to CC grew the colonies. The growth, at first feeble, with few colonies, became more dense further away from the Prontosil (Fig. 5). Da and Da represent the distances in which the growth was completely inhibited in the 1/1 broth in the control and ionized plates respectively. It is noticeable that Da was appreciably greater than D1. Again, the colonies were far fewer in the ionized plate than in the control. One other point is that D3 and Dc are shorter than D2 and Db. In other words the range of inhibition was losing power of effective efficiency.

In the ionized plates the Prontosil was driven away $\frac{1}{8}$" from the positive electrode leaving the agar free from the azo dye constituent. No migration of Prontosil was observed

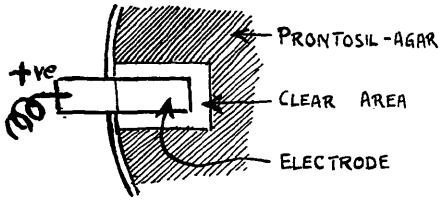


FIG. 6.

at the line of demarcation. FIG. 6.

CONCLUSIONS Prontosil inhibits the growth of staphylococcus aureus. The fewer the germs, the greater is this power. Ionization very considerably increases the power of inhibition.

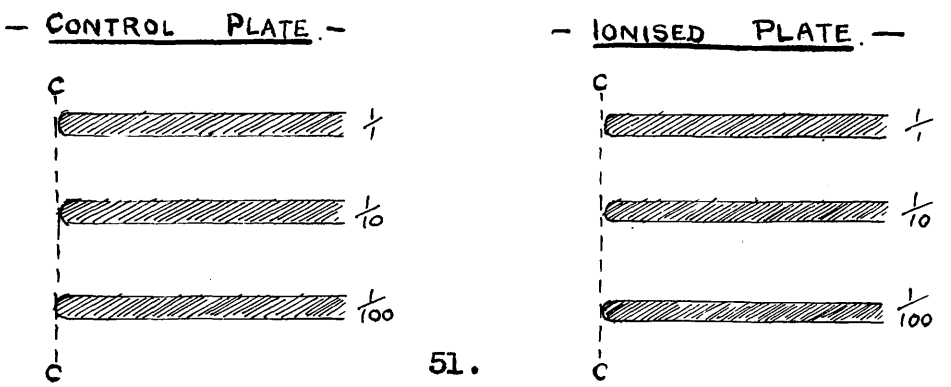
Prontosil, or at least the ago dye constituent, is forced towards the nagative pole.

EXPERIMENT No. 7.

In the last experiment it was found that ionization with Prontosil greatly enhanced the inhibition of growth of the bacteria. This might be due to the current alone and not to current plus Prontosil.

Two Agar Plates were therefore prepared, one having tin electrodes implanted as in the previous experiment. No Prontosil was used. Smears were drawn across the plates, of a broth containing Staphylococcus Aureus and also dilutions 1 in 10 and 1 in 100, as in Experiment 6. The plate with the electrodes was subjected to a Galvanic current of 10 M.A. for 5 minutes. Both plates were incubated for 24 hours.

RESULTS A diagramatic sketch of the results constantly secured in several tests is shown.

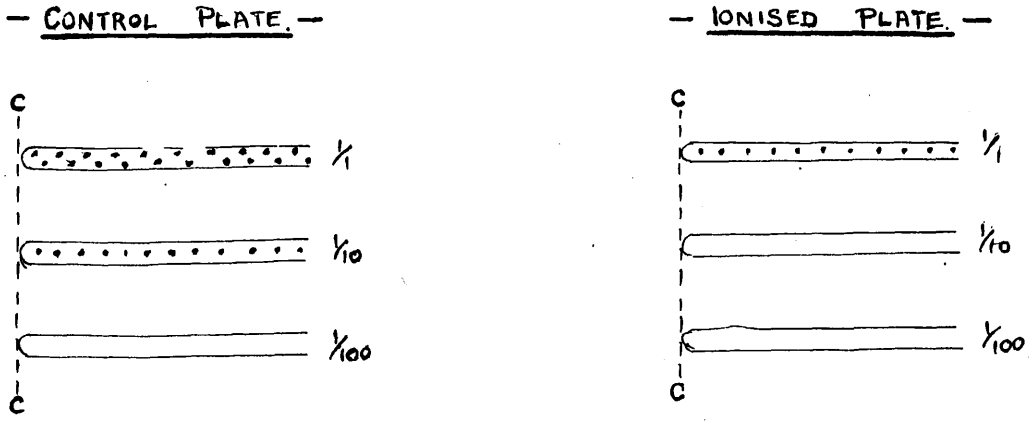


No difference between controls and ionised plates could be distinguished. The growth was not interfered with by the electric current.

CONCLUSIONS. The Galvanic current alone does not inhibit the growth of Staphylococcus Aureus. Hence in Experiment 6 the increased inhibition of growth is due to ions of Prontosil when carried over by the current, affecting the germs and preventing their growth.

EXPERIMENT No. 8.

As a control over the Prontosil itself, plates of agar containing 1% of a 2½% Standard Prontosil solution were prepared. One had terminals implanted into the Prontosil Agar. Smears of Staphylococcus Aureus broth 1/1, 1/10, 1/100 were drawn across the plates as in Experiments 6 and 7. The electrode fitted plate was subjected to a Galvanic current of 10 M.A. for 5 minutes. The plates were incubated for 24 hours.



The strength of growth is diagramatically represented above. No growth was visible in either plate of the dilution 1/100. There was no growth in the 1/10 dilution.

after ionization but some scattered colonies grew in the control. The full strength broth after ionization was feeble in growth. Scattered colonies only survived. The control growth, though sparse, was very much more dense than on the ionized plate.

CONCLUSIONS. Prontosil per se inhibits the growth of Staphylocuccus Aureus, especially when the implant is small. Ionization enhances this power of inhibition.

EXPERIMENT No.9

The preceding experiments have shown the power of inhibition of growth of bacteria possessed by Prontosil and its enhancement by ionization. The same type of plate as used in Experiment 6 was made, part of the Agar being replaced by Agar containing Prontosil and electrodes were introduced. Staphylococcus Aureus smears were drawn across in a similar manner and in similar strengths. These were incubated for 24 hours. The Galvanic current was passed for three hours at 15 M.A. to see if any of the growth thus established was affected.

RESULT. No change was observed in the cultures. The growth in all cases showed no destruction.

CONCLUSION. Prontosil per se and after ionization does not possess any power to destroy Staphylococcus Aureus in vitro.

REMARKS. The behaviour of the Prontosil during and after ionization is worthy of note.

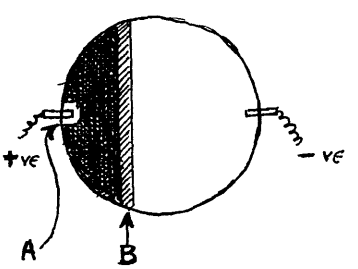


FIG. 1.

After 15 minutes the Prontosil had been driven away from the positive electrode at point 'A' Fig 1 a distance of nearly ¼". At 'B', on the Agar side of the line of demarcation, Prontosil had

travelled towards the negative pole staining the Agar a faint pink.

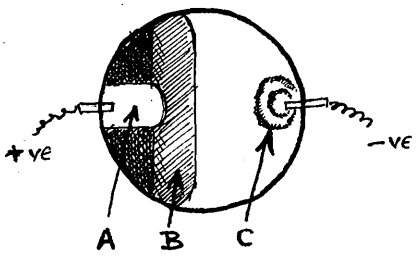


FIG. 2.

After three hours ionization, the clear area 'A' around the positive pole had extended past the line of demarcation. The area 'B' had spread towards the negative electrode a distance of 1" beyond the line of demarcation. The formation of these two areas is indicated in Fig. 2. At 'C' two brownish concentric rings had formed. Twelve hours later 'A' was open towards the negative pole, 'B' had been separated into two distinct separate areas, whilst at 'C' the brownish rings were still evident but were enveloped in a pinkish cloud, Fig. 3.

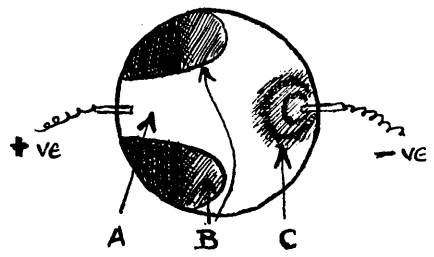
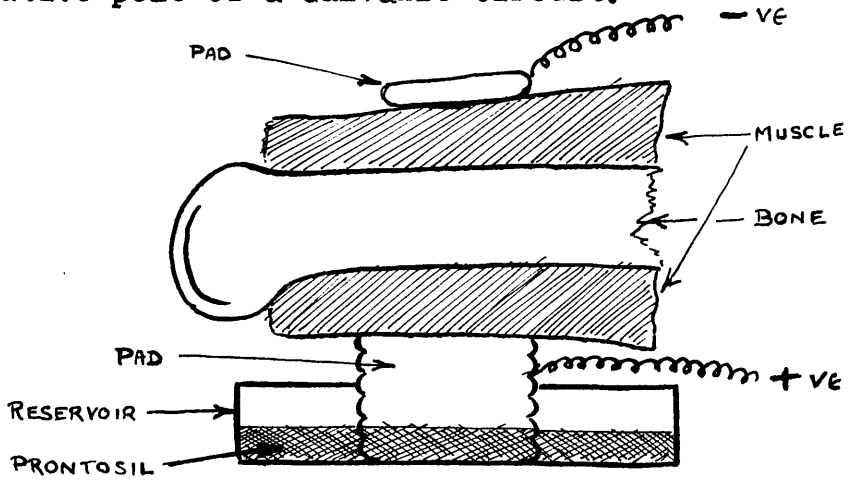


FIG. 3.

CONCLUSION on Experiments 6, 7, 8, & 9 These experiments show that Prontosil is bacteriostatic and is not bacteriocidal. Ionization increases in a marked degree the former power and does not influence the latter.

EXPERIMENT No. 10.

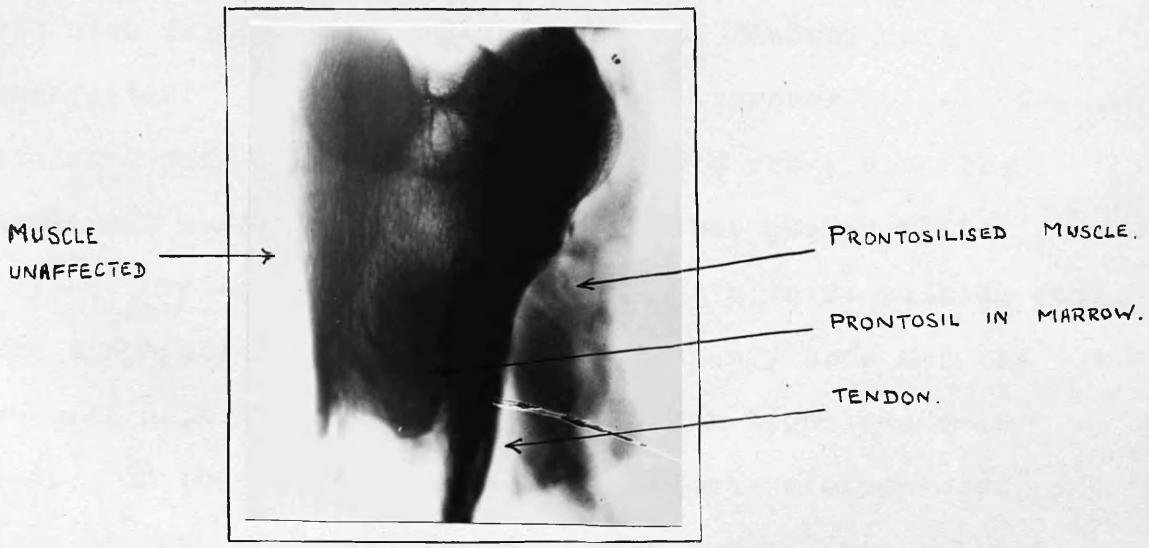
On finding that Prontosil was to some extent opaque to X-rays, the knee joint of a piece of lamb was used in this experiment. The muscles around the bone having been laid bare, a pad of lint, moistened with sodium chloride was applied to its surface and attached to the negative pole of a Galvanic circuit.



Diametrically opposite, a little pile of pads moistened with 2½% Prontosil was applied to a raw surface representing a wound. This collection was attached to the positive pole. The pads were kept in position by elastic bands, and to keep the Prontosil pads moist throughout the experiment, they rested in a supply of this solution in a small basin.

This arrangement was made as the Prontosil was not markedly opaque to the X-rays, and therefore, to have a visible X-ray picture, the current would have to pass for some time. Thus the pads were prevented from becoming dry during the experiment. 100 milleamperes were passed for four hours. An X-ray film was then taken.

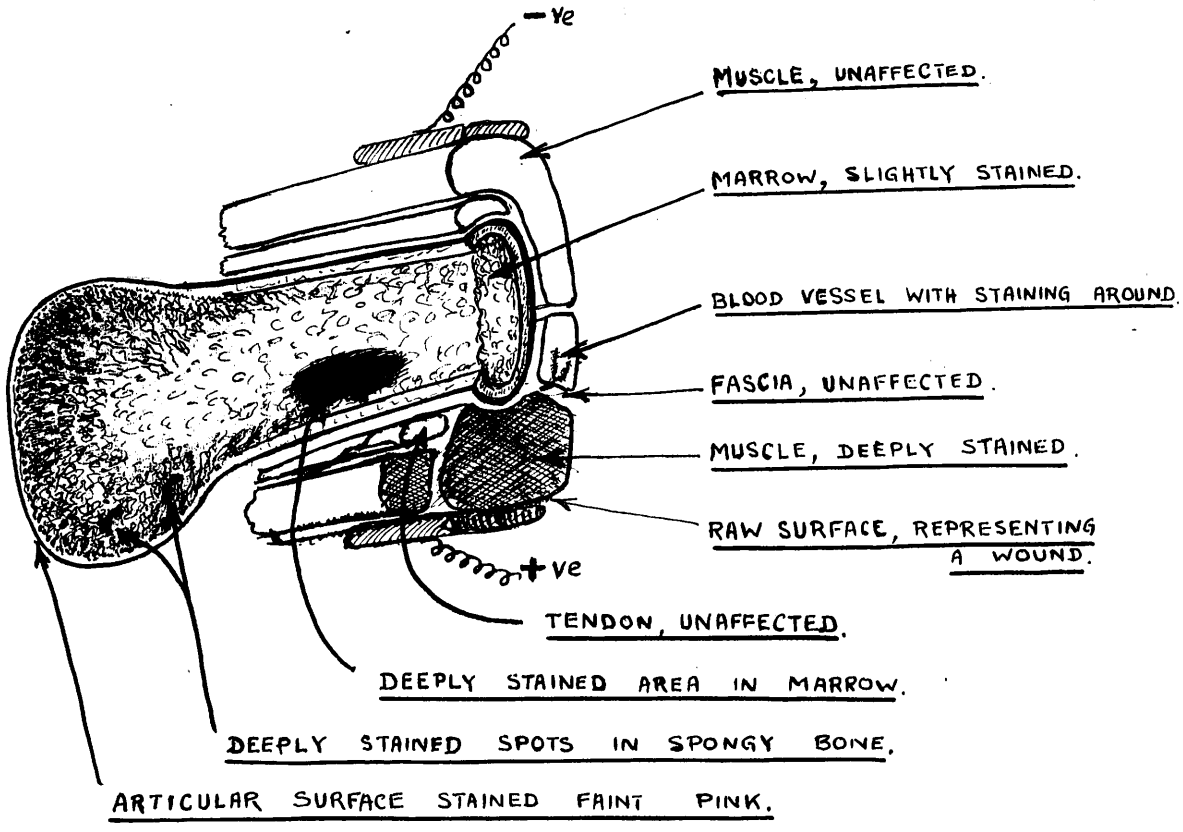
RESULTS (a) X-ray



The print, from the X-ray plate shows that the Prontosil has been forced into the substance of the muscle. The muscle under the negative pole was uneffected. The shadow in the bone itself was due to a dense infiltration

of Prontosil. No information was gained from the X-ray film which was not found on dissection. It is, however, a visual confirmation.

(b) Visual. On dissecting the meat, the muscle was very deeply dyed with the Prontosil on the postive pole side of the bone. The fascial layers were stained on the side adjacent to the muscle but the Prontosil had not been forced through. The fibrous tendons were unaffected. Through these surfaces, however, rings of staining were readily seen around blood vessels. The articular surface of the bone, which was pearly white before treatment, was now glowing with a faint pinkish hue. The diaphysis was unaffected. The spongy bone and the medulla ossium were uniformly stained a light shade of red. In the medullary cavity the deeply stained area, seen in the X-ray, was found to have spread from a blood vessel thus accounting for its origin. In the spongy bone a few deeply stained spots burrowed into the bone - Prontosil passing along blood vessels before dissemination.



CONCLUSION. From a raw surface, Prontosil is ionisible deeply into the substance of mammalian muscle. It passes alongside blood vessels through fascia. In this manner too, it passes into bone where it diffuses in the marrow. Confirmation of most of these statements is shown in the X-ray print.

EXPERIMENT 11

Attempts were made to X-ray the rate of penetration of Prontosil into mammatian muscle. The opacity of Prontosil was not sufficiently dense to gain this object. Confirmation of the previous experiment was all that was secured.

CASES.

C A S E S.

In the Section on Ionization it has been shown that drugs are forced into the tissues, and confirmed in the Experimental Section that this holds good in the case of Prontosil. Again, in the chemotherapy section numerous reports show that sulphanilamide, used locally, is likewise a powerful weapon in mastering many pathological conditions. Combined use of two such effective methods should, it is reasonable to expect be more effective than either used separately.

Every case which was given treatment is included in the following reports. The cases have been grouped according to the type of lesion treated. The group classification of each case is indicated at the top right hand corner of each page. The number quoted is the chronological number, or order of appearance at the Physiotherapy Department.

To save repetition in the reports, each lesion was cleansed and irrigated with Hydrogen Peroxide 1 in 4. The ionizations were given twice or thrice weekly. This routine treatment was commenced on 12th April, 1940. With regard to the use of Peroxide of Hydrogen, Mayo and Miller (68) on 25th September 1940, reported that, in the Mayo Clinic, they found the

previous use of this lotion, before the application of sulphanilamide was more efficacious than the application of sulphanilamide alone.

For superficial wounds, a pad moistened with Prontosil was used as the anode. Deep abscesses, after thorough irrigation with hydrogen peroxide, had the cavity filled with Prontosil and moistened ribbon gauze packed in around the positive electrode. A vulcanite speculum was used to treat ear cases and this instrument was kept filled with Prontosil. With nose cases, moistened ribbon gauze was packed up the nasal passages and, when the antral cavity was being treated, a cannula was left in situ and kept filled. By this means the antrum was ionised throughout.

Instead of writing mille-ampere each time, the abbreviation M.A. is used.

Case No. 1.

Name Mrs. B. Age 21. Occupation Shop Assistant.

History of Lesion A paronychia developed in December 1939. The nail was removed and the usual dressings applied. A new nail grew one third of the normal length, but was soft and oozed pus. Cleansings with hydrogen peroxide, mag. sulph. compresses, Kromayer lamp treatment and zinc ionization were all tried.

Condition - 1st attendance. 12/4/1940. The nail was soft and pus was readily expressible.

Pus No examination was made. This was the first trial of the method of treatment.

Ionization 3% Prontosil was used at 3 mille-amperes (3 M.A.) for 10 minutes under the positive pole.

Result 19/4/1940 There was no pus; the nail was healthy and firm

Treatments given Two.

Follow-up One month later the nail was still growing and was still healthy. She could not be traced in 1941.

Case No. 2.

Name Mrs. H. Age 47 Occupation Housewife.

History of Lesion. This patient had a septic elbow for four or five years. It seemed to be healing but would then break down again.

Previous treatment. Foments, poultices and sulphanilamide orally had all been tried.

Condition - 1st attendance. On 9/5/1940 there was a large fluctuant area over the radius for 5" below the elbow, 3" wide, and deep in the tissues. Pus oozed from three sinuses, each ½" or more in diameter.

X-ray No disease of the bone was seen.

Pus A mixed infection was present.

Ionization 3% Prontosil at 4 M.A. for 10 minutes was used.

Result. After five treatments, the tissues were firm and the sinuses were healing. Fifteen further treatments resulted in perfect healing except for one sinus which was over the acromian process and was only skin deep. The arm was placed in a sling to prevent excessive movement. It later healed.

Follow-up The arm was inspected at frequent intervals.

On 12/12/1940 an ulcer was present which looked syphilitic. The Wassermann Test was "strongly positive "1 in 32". It healed with Pot Iod. and has remained so up to 1/8/1941.

Treatments given. Twenty.

Remarks. The ionization had quickly cleared up the staphylococci and streptococci. The specific infection had caused the delay in healing. Sezary (48) cured soft chancres with sulphanilamide locally applied, but no mention of syphilitic lesions being treated in this way has been found in the literature by me. The result here obtained may be a coincidence but is nevertheless interesting.

The chronocity of the case and the failure of her own doctor's treatment with sulphanilamide orally was due to the point mentioned in the War Office Memorandum of 3/7/40, p. 10 - "The drug has but little effect when septicaemia arises from an ineradicable purulent primary focus." There was no septicaemia in this case, but the concentration of the drug in the blood stream by oral treatment was insufficient to control the infection in the ineradicable focus.

Case No. 5

Name Mrs. W. Age 45 Occupation Linoleum Worker.

History of Lesion On 12/7/40 a wagon ran against her left Tibia.

Previous Treatment Fomentations were applied for a month at the Work's ambulance room.

Condition - 1st attendance. 14/8/40. In the middle third of the left Tibia was a swelling 2" x 1½", oozing pus.

Pus Staphylococci and Streptococci.

X-ray Periostitis.

Ionization 2½% Prontosil was used for 10 minutes at 6 M.A.

Treatments given Four.

ResultAfter the first treatment, the pus became thin and the pain and swelling less. It had healed by 24/8/40 after four treatments.

Follow-up 14/9/40 Leg normal.

Remarks A thorough irrigation with hydrogen peroxide was readily and effectively carried out and so there was not much pus present when the ionization was given. From clinical experience I am confident such a lesion would not have cleared up so quickly with peroxide of hydrogen alone, nor with the usual dressings.

Case No. 9

Name Mr. C. Age 31 Occupation Office Manager.

History of Lesion For one week this patient had had a carbuncle on his neck.

Previous treatment Poultices, 1½" cross incision, foments, sulphanilamide orally had been tried.

Condition - 1st attendance. By 23/10/40 the Carbuncle was about 2" diameter, the pus was cheese-like.

Pus A mixed infection was found.

Ionization 5% Prontosil for 10 minutes at 4 M.A. was used.

Treatments given Three.

Result On 26/10/1940, after the first treatment, the pus oozed freely. On 28/10/1940 the base was clean and dry, and after a third treatment, the wound was practically healed.

Follow-up One month later, it was difficult to detect where the carbuncle had been.

Remarks. I estimate that this huge carbuncle healed in about a third of the time it would normally have taken.

Case No. 10.

Name Mr. H. Age 55 Occupation Air Raid Warden.

History of Lesion He had a septic finger in 1937, a septic toe in 1938 and repeated abscesses which took months to heal.

Present lesion - an abscess of a heel of nine months duration.

Previous Treatment Sulphanilamide per os. Foments and poultices.

Condition - 1st Attendance. 2/10/40. In the middle of his right heel was a sinus ¼" diameter widening out funnel-wise to a depth of 1½". Copious pus was oozing from the opening.

Pus Pus cells, some staphylococci and gram negative diplococci.

X-ray Bone necrosis of posterior edge of Os Calcis

W.R. Negative.

Ionization For 10 minutes 2½% Prontosil was ionized into the cavity at 4 M.A. - 15 M.A.

Treatments given Twenty-one.

Result After four treatments he walked freely, without limping. There was no pus but the wound had not healed.

A further six treatments and the wound had healed enitrely, but the heel had become tender at the side. At his next attendance another sinus had developed down to the bone.

Two treatments were given and he was sent home to rest for a week. It had healed by 1/4/40.

For a later sinus nine treatments were required.

Follow-up 6/1/41 and 19/7/41. No further trouble.

Remarks. The sinuses healed quickly but the source of infection had not been effectively reached until the third sinus made its way to the surface, and was ionised. This would appear, from the history, to be blood borne infection. Confirmation would seem definite on account of the formation of another abscess, the history of which has been entered as a separate case (19). Where freedom for free ionization is difficult, such as a narrow sinus, this case and some to follow show rapid healing of the sinus and outer layers of the wounds, for no inconsiderable depth, but pockets of infection have been thus formed.

Case No. 14.

Name Mr. H. Age 86 Occupation Retired

History of Lesion About six months previously an abscess had developed on the sole of this patient's left foot.

Previous treatment Fomentations.

Condition - 1st attendance 15/7/40. There was an abscess about ½" in diameter on the sole of his foot. It burrowed in under the skin. The course was tortuous and the depth could not be ascertained.

Pus Mixed infection.

Ionization 2½% Prontosil was used for 4 minutes at 3½ M.A.

Treatments given Two.

Results Two treatments only were given. Pus had ceased to ooze from the opening but he became ill with another complaint and later died but not before the abscess had healed - by the 14/8/40 - just one month after the first treatment.

Remarks Although the abscess had been cured, it might not have been a permanent cure if the man had lived. Apparently it looked a perfect cure on the date on which his doctor reported.

CASE No. 19

Name Mr. H. Age 55 Occupation Air raid warden.

History of Lesion See also Case 10. On this occasion this man's right elbow had been discharging pus all summer (for six months).

Previous treatment self dressings.

Condition - 1st Attendance 6/11/40. An ulcer about an inch in diameter was present at his right elbow. A sinus made its way into the flesh for at least an inch. Much pus was present.

Pus Mixed growth including dipheroid bacilli.

Ionization For 10 minutes 5% Prontosil was used at 4 M.A.

Treatments given Ten.

Result The sinus had healed completely by 15/11/40 when he had had four treatments. The ulcer was considerably smaller and healthy granulations were showing.

By 6/12/40 the skin had healed across the wound - six further treatments having been required.

Follow-up 6/1/41 and 19/7/41 the elbow had remained trouble free.

Remarks His doctor reported that normally this ulcer would have been active for many months.

A six month's activity was cured in ten treatments

Case No. 21

Name Mr. H. Age 35 Occupation Labourer.

History of Lesion Thirty one years ago this man had osteo-myelitis of his left femur and tibia. The knee was ankylosed and the leg shortened and wasted. Seventeen years later he was in Leeds General Hospital for one year and had several operations on account of a re-awakening of the osteo-myelitis.

The knee began to swell and became inflamed in October 1940.

Previous Treatment Kaolin poultices.

Condition - 1st Attendance 4/12/40 On the medial aspect of his left knee there was a large swelling about 3" x 2" which was raised about 1" from the surface. There were two openings exuding pus.

X-ray Old osteo-myelitis of knee joint. Area of rarefaction lower end of femur shaft. ? site of new infection.

Pus Pneumococci and staphylococci

Ionization For 10 - 20 minutes 5% Prontosil was used at 5 - 10 M.A.

Treatments given Fifteen.

Result Following eight treatments, the condition had improved. There was now no inflammation; the dressing was only tinged with pus. Seven more

were given when complete healing was attained.

Follow-up Seen at frequent periods until June 1941.

The knee had remained quiet and caused no trouble.

Remarks. Clinically, at least, this was an established periostitis. X-ray was not definite. In any case an abscess was cured and possibly a bone infection prevented if not also cured.

Case No. 24

Name Mrs. T. Age 31 Occupation Housewife.

History of Lesion Mrs. T. suffered from a pilonodal abscess which had been oozing pus for 1½ years. Operation had not been successful.

Previous treatment Excision had been carried out over the mid line of the sacrum.

Condition - 1st Attendance. On 8/1/1940, two sinuses were present at the ends of the 6" operation scar. They were 1½" deep and about the size of a pigeon's egg under the mouths of the sinuses which were only ¼" in diameter. There was a connecting passage under the scar.

Pus Streptococci only were present.

X-ray This showed no bony disease.

Ionization 2½% Prontosil was used fro 15 minutes at 15 M.A.

Treatments given Forty-five.

Result The cavities soon became smaller, (¾" deep and ¼" in diameter) and had to be kept open for treatment of the long connecting fistula. Eventually it was decided to have this laid open

and treat as an open gutter. Unfortunately excision was performed and the incision sutured. Soon afterwards pus was being discharged again.

Remarks. The large cavities had almost filled up but were deliberately kept open. The skin especially was stimulated to much growth. The difficulty in treatment was to fill the fistula with Prontosil. I cannot but feel that if my wishes had been carried out, the abscess would have healed.

Case No. 28

Name Bessie G. Age 12 years Occupation Schoolgirl

History of Lesion An operation for a ruptured appendix was performed on 27/11/1940. From the site of the tube pus had been discharging for over two months.

Previous treatment. In addition to the usual dressings, sulphanilamide had been given orally.

Condition - 1st attendance On 28/2/1941, at the lower end of the para-median incision, a sinus 1/3rd in. in diameter was present. This tracked upwards, ever widening for about 4". The area was quite fluctuant.

Pus Streptococci and staphylococci were found on culture.

Ionization 2½% Prontosil was ionised into the wound at 15 - 20 M.A. for 10 - 15 minutes.

Treatments Eighteen treatments.

Result By 22/2/1941 the wound had healed.

Follow-up On 11/8/1941 this girl had had no further trouble

Case No. 31

Name Sylvia R Age 5 Occupation Schoolgirl

History of Lesion A suppurating gland on the right side of her neck had been incised by her own doctor but had discharged for over a year.

Previous treatment Poultices before, and dressings since the incision.

Condition - 1st attendance 27/3/41. A 1" scar was present on the right side of this child's neck. ½" of this scar was thin skin. Typical cheesy tubercular pus was expressed from an opening in the thin part of the scar.

Pus No organisms found.

Ionization For 15 minutes 2½% Prontosil was ionised in at 10 M.A.

Result One treatment only was given. She could not attend on account of chickenpox.

Follow-up The wound had healed one week after treatment. When seen on 6/5/41 the skin over the wound was firm and healthy.

Remarks This is the first tubercular lesion treated with Prontosil. No claim can be based on this mild

case. Certainly the result of one treatment is interesting, and suggests that further tubercular abscesses should be similarly treated as Ultra-Violet Rays would not have been so quickly effective.

Case 33

Name Mrs. W. Age 27 Occupation Housewife

History of Lesion. A swelling developed over her left lowest rib in November 1940.

Previous Treatment An operation was performed in December 1940. The abscess was very deep seated, the source not being found.

Condition - 1st Attendance. 20/5/41 . An unhealed incision 3" long was present over the patient's left lowest rib, commencing 2" from the mid line of her spine. The muscle had healed but not the skin and there was a crater-like opening in the wound ½" in diameter from which pus was running. This sinus burrowed in for at least 4".

Pus Repeated cultures grew no organisms.

X-ray December 1940 - Shadow over left kidney area.
May 1941 - Cannot detect any evidence of bone involvement.

Ionization 2½% Prontosil was used for 5 - 15 minutes at 5 - 10 M.A.

Treatments given Forty four

Result By 20/6/41, after eight treatments, the incision had healed to 1" around the sinus which was now only

a small opening and about 1½" deep. No side tracks could be felt. The wound around had healed on 8/7/41, the sinus was 1" deep, the opening about half the thickness of a pencil - six further treatments had been given. 12/8/41 the patient's health was very much improved. She had not felt so well for years. The sinus was still 1" deep but was narrowing. Thirty treatments were again given before this small sinus eventually healed entirely. Of these treatments a good number were given for a very small lesion which would normally be left to heal on its own. The skin was complete on 24/9/41

Follow-up On 4/11/41 Mrs. W. returned as the wound had shown signs of discharging. There was very little discharge actually; the sinus had remained healed, the skin only was broken of the wound for 1/3rd inch. Good healing took place after a few treatments. 2/12/41. Still satisfactory.

Case No. 35

Name Mr. D. Age 47. Occupation. Ship's steward.

History of Lesion In September 1940 this man suffered from pain in his right kidney region and was treated for rheumatism and neuritis until February 1941 when a swelling came up lateral to the right kidney area.

Previous treatment Operation. The swelling was opened and found to be an abscess, so deep that the source was not traced. The kidney was healthy. A gangerous condition of the skin supervened. His condition was given up as hopeless. For the last month, the wound was not looked at, the sister having been told to do whatever she liked.

Pus Pneumococci, short chain streptococci, gram positive bacilli encapsulated (? Gas gangrene)

X-ray ? Neoplasm affecting ascending colon. (After operation his constipation was relieved, there were never any abnormal contents in his faeces)

Condition - 1st Attendance 13/6/41 A large area roughly 12" x 12" denuded of all skin and subcutaneous tissue

was present. It stretched over ribs, abdomen, back and down over the ilium. The edges were undercut, the muscles were showing, sweltering in foul pus. Two sinus, 2" in diameter were like cauldrons of pus.

Ionization 2½% prontosil on gauze was ionised in for 15 minutes at 12 - 25 M.A.

Treatments given Four

Result After the first treatment the patient said he had much less pain and was truly more comfortable than he had been since he entered the Infirmary. By the end of the fourth treatment the wound was dry. Anteriorly the edges of skin and subcutaneous tissues were no longer undercut but sloped down to the muscles of the abdomen, were free from pus and looked really healthy. Towards the spine and over the ilium, pus was still present and squelshed out from the still undercut skin. The sinuses were discharging ever so much less pus. Circumstances arose which made further treatment impossible. The wound became as bad as ever and the man died on 27/7/1941

Remarks The retardation of the diseased part under the treatment had been better than expected. More than half the edges had become healthy and the base was dry. The toxic condition had been improved. It is difficult to speculate or visualise what the outcome would have been if he had lived, the destruction of tissue had been so extensive

Case No. 41

Name Joseph L. Age 11 Occupation Schoolboy

History of Lesion This boy was an evacuee and apparently had a T.B. hip and an operation on the joint when quite young. He came to Lancaster in January 1941 with a discharging sinus below the Great Trochanter.

Previous Treatment Dressings at the school clinic.

Pus T.B.

Condition - 1st Attendance. 29/7/41 About 2 " below the Great Trochanter was an area of inflammation ½" diameter, raw and covered with cheezy pus from the opening of a sinus ⅛" wide.

Treatments given One.

Ionization One treatment was given with 2½% Prontosil at 10 M.A. for 1 0 minutes.

Result For three days pus came freely from the sinus. His temperature rose to 101° , when he was sent to hospital

Conclusion It would seem that the treatment was the spark which caused a flare up. On the other hand it may have been coincidental. In any case, no benefit was achieved (unless the fact that it made the pus thinner and discharge freer be so described).

Case No. 44.

Name Mr. W. Age 18 Occupation Joiner.

History of Lesion His left hand was injured at work, on 14/9/41. The wound became septic and the hand very swollen.

Previous Treatment Tablets (sulphanilamide) internally, fomentations, and dressings with powder (sulphanilamide) had been used.

Condition - 1st Attendance. 6/10/41. The hand was considerably swollen, pus was discharged in large quantities from two wounds 1" x ½" and ½" x ½" in the 3rd - 4th inter-metacarpal spaces. The wounds were deep and about 2" apart.

X-ray No bony involvement.

Pus Staphylococcus Aureus.

Ionization. This was given at 10 - 20 M.A. for 15 - 20 mins. with 2½% Prontosil.

Treatments given Fourteen

Result The wound healed satisfactorily and there was no limitation of movement by 7/11/41.

Case No. 49

Name Mr. C. Age 75 Occupation Retired engine driver

History of lesion For 36 years he has had ulceration of his Right leg. His left leg was amputated in an accident a short time before the ulceration began.

Previous Treatment Ointments, lotions, elastoplast, tulle gras.

Condition - 1st Attendance. 4/11/41 An ulcerated band ran round the leg above the ankle but did not quite meet by about 3". In depth it varied from ¼" to ½". The tibia was swollen over its anterior surface.

Pus. Staphylococci and Pneumococci

X-ray "Condition of Periostitis involving greater part of the Tibia"

W.R. Negative

Ionization 2½% Prontosil was utilised at 25 M.A. for 20 minutes.

Treatments given Twelve

Result The ulceration has almost healed (7/12/41)

Follow up He is still under treatment.

Remarks Although the wound is practically healed, the tibia is still swollen. The tissues feel and now look healthy over the whole length of the bone.

Case No. 50

Name Mrs. A. Age 60 Occupation Housewife

History of lesion An operation on both great toes was performed in London in August 1940. The right toe has discharged ever since.

Condition - 1st Attendance 14/10/41. The incision scar was ballooned up as thick as a No. 12 catheter. The scar was fluctuant and pus was expressed from a ¼" sinus. A probe showed that this sinus was at least 1½" deep.

Pus Staphylococci and Pneumococci

X-ray Small sequestrum of bone present.

Ionization was given with 2½% Prontosil at 3 M.A. for 15 minutes.

Treatments given Five.

Result After these treatments, the wound healed then broke down again. X-ray examination was then made. In view of the report she was admitted for operation.

Follow-up The wound healed by first intention and has remained so.

Remarks. By treatment the wound became clean and healed The breakdown which followed was due to the

sequestrum. No ionization, or treatment other than removal, could therefore clear up the condition. It is interesting that it healed at all.

Case No. 52

Name Mrs. A. Age 45 Occupation Housewife.

History About five months ago she had a septic hand which resulted in loss of sensation and stiffness of the fingers.

Previous treatment Wax baths and massage were given.

Condition - 1st attendance The second and third finger tips were burned in the wax, the nails were floating on bags of pus. The nails were removed on 2/10/1941. The terminal phalanx bones were projecting, two thirds being unprotected by any muscle.

Pus Staphylococci.

Ionization This was commenced on 8/11/41 using 2½% Prontosil at 5 M.A. for 15 minutes.

Treatments given Nine (9/12/41)

Result The fingers are free from pus. The flesh now covers the bones. The new nails are commencing to grow.

Follow-up She is still under treatment.

Remarks. This has proved a very satisfactory case. The nerve supply had been so affected that she sustained burns and yet has shown rapid healing under ionization.

Case No. 54

Name Miss W. Age 46 Occupation Milliner

History of Lesion Pain had been suffered in the left breast for about five months.

Previous treatment Amputation of the breast was carried out on 7/10/1941, a tumour having been found. The usual dressings were applied.

Condition - 1st Attendance. On 2/12/1941 the incision was not healing at two areas. One gap was $2\frac{1}{2}$" long by 1" wide, the other 1" long by $\frac{1}{8}$" wide.

Pus Mainly staphylococci

Ionization $2\frac{1}{2}\%$ Prontosil was again used at 20 M.A. for 10 minutes.

Treatments given One

Result No improvement in the few days which have elapsed, has been noticed, except that the wound is cleaner. No more could be expected.

Follow-up She is still under treatment.

Case Reported by W.H. Woods F.R.C.S., Swansea Hospital

A man aged 47, a clerk by occupation, was first seen 14/5/36 with a swollen elbow following chronic pleurisy. The arm was opened over the olecranon and sterile pus was found. The infection spread over the posterior aspect of the arm in its upper third, was about 4 " wide, and was deep in the tissues and boggy. Contracture of three fingers and septic sores developed. It healed on occasions only to break down. In 1938 long chain streptococci were obtsined and autogenous vaccine treatment undertaken, improvement only being obtained.

Ionization This was commenced on 10/7/40 with 2½% Prontosil and the abscess was completely healed on 11/12/40 after 41 treatments.

Result Cured.

Case No. 3.

Name Harry B. Age 10 Occupation Schoolboy

History of Lesion For more than 12 months this boy had a profuse, offensive smelling nasal catarrh.

Previous Treatment Sulphanilamide per Os.

Bi-weekly antral wash-outs for 6 months.

Condition - 1st Attendance. 28/6/40 There was a copious discharge from his nose. The nose was very swollen. His upper lip was twice as thick as the lower lip and almost touched his nose.

Pus. Profuse growth of Staphylococcus Aureus.

Ionization Following the antral wash-out ionization was given of 3% Prontosil for 10 minutes at 4 M.A., using the antral cannulæ for filling the antra with solution, then packing Prontosil soaked gauze into the nose.

Result By the third treatment the swelling had practically subsided. No discharge occurred after the last treatment.

Treatments given eleven

Follow-up Since his discharge he had remained free from catarrh up to 11/8/1941

Case No. 4.

Name John N. Age 5 Occupation Schoolboy

History of Lesion Otitis media of over one year's duration.

Previous Treatment A mastoid operation was performed soon after the ear began to trouble this boy. Zinc ionization had been carried out on 39 occasions. At times it seemed to be drying up, then a relapse took place.

Condition - 1st attendance. On 2/7/1940, pus filled the orifice of the affected ear.

Pus Mainly streptococci were found on culture but some staphylococci were present as well.

Ionization For 10 minutes 2½% Prontosil was ionised in at 2 - 4 M.A.

Treatments given six.

Result The discharge had been very much reduced when he ceased to attend. He could not be traced until 15/7/1941 when the report was that there was still some discharge but it was very little.

Case No. 7.

Name Mrs. P. Age 23 Occupation Housewife

History of Lesion One ear had discharged pus for 9 years following Scarlet Fever.

Previous Treatment This had consisted of "ear drops"

Condition - 1st Attendance. 15/10/40 The affected ear was filled with pus.

Pus Mainly streptococci

Ionization Six treatments were given with 2½% Prontosil at 5 M.A. for 7 - 10 minutes.

Result After 4 treatments there was no sign of any pus. Serous discharge on 1/11/40 ran down her face after a treatment. Seen at the end of the same month, there was no discharge, and this has continued until November, 1941.

Treatments given Six.

Remarks. In this case the perforation in the drum was large and allowed effective contact and treatment to be carried out.

Case No.11.

Name Mr. T.R.H. Age 25 Occupation Cabinet Maker.

History of Lesion. This man's right ear had discharged for five or six years.

Previous Treatment Ear drops.

Condition - 1st attendance. 7/10/1940 The floor of the aural passage was covered with pus.

Pus Streptococci and staphylococci

Ionization Treatment was given with 2½% Prontosil for 7 minutes at 3 M.A. for six treatments. There was very little discharge. 5% Prontosil was used on the next occasion but this resulted in pain and watery discharge. The subsequent eight treatments were given with the weaker solution.

Result No discharge.

Treatments given Fifteen.

Follow-up In December 1940, the ear had caused no trouble whatever. He was accepted for the Army, being passed A 1. On 4/8/1941 he reported that his ear had never discharged since his treatment.

Remarks 5% Prontosil would appear to be too strong for ionising ears, and results in a catarrhal condition.

Again, the previous case also showed the same result after an ionization where there was no pus. The spacing of treatments and the strength of the solution requires much further observation.

Case No. 12.

Name Mrs. D. Age 53 Occupation Housewife

History of Lesion She undertook in June 1940 the care of an evacuee, who was always snuffling. She soon developed a "nasty" nasal discharge.

Previous Treatment Sulphanilamide per Os.
Partial resection of septum
Bi-weekly antral wash-outs.

Condition - 1st Attendance. 7/10/40. Thick pus from the antrum oozed into the nose. A patch of membrance was present on one middle turbinal. No swab had ever been taken.

Pus 7/10/40. Mixed infection with many bacilli. Sub-culture - K.L.B.

Ionization After irrigation the cannula was left in situ, and 2½% Prontosil instilled, with packing into the nose; ionization for 7-15 mins. at 2½ M.A. was given.

Result After 6 treatments the swab was practically free. Four further treatments were given. On these occasions, no K.L.B. were found.

Follow-up One month and about three months later, she had no catarrh of any kind. 16/8/41. The nose was clear.

Treatments given. Ten.

Remarks. One treatment stopped the free nasal discharge.
Each further treatment reduced the growth of colonies of germs on culture.
Seven treatments rendered the nose K.L.B. free.
The third culture consisted of staphylococcus Albus and K.L.B., the streptococci had disappeared, apparently therefore, streptococci being more susceptible to Prontosil than staphylococci.
Mention may be made regarding the reversibility of streptococci and dipheroids which is here a possibility (Mellon (33)).
In view of the report on sulphathiazole snuff (Payne & Auchinleck, (67) Ionization is not suggested as a possible treatment for all nasal diphtherias but might prove useful in refractory cases.

Case No. 13.

Name Bessy O. Age 14 Occupation Schoolgirl

History of Lesion This patient had scarlatina at the age of ten and had been troubled with nasal discharge ever since.

Previous Treatment For 10 months, bi-weekly antral washouts, sulphanilamide per Os and instillation of prontosil had been tried.

Condition - 1st Attendance 3 /10/40. The lining of the nose was very congested; much thick discharge was present.

Pus 3/10/40 Staphylococci, streptococci pneumococci
9/11/40 Mixed infection - some diphtheroids but mainly Hoffmann's Bacilli.

Ionization 5% Prontosil at 3½ M.A. for 4 - 6 minutes for six treatments gave no beneficial result. One ionization with zinc sulphate was now tried but resulted in an increase of discharge. Four further Prontosil treatments were given.

Treatments given Ten

Follow-up No improvement up to 16/8/41.

Remarks. There is no obvious reason why zinc ionization should have caused an increase in the catarrh, and may have been coincidental. It would appear that Hoffman's bacillus is not affected by Prontosil. The staphylococci streptococci and pneumococci had been almost obliterated.

Case No. 15.

Name Mrs. C. Age 63 Occupation Housewife.

History of Lesion For many years, nasal catarrh had been constantly present and had been very severe for the past seven months.

Previous Treatment Large Antral openings had been made and daily irrigation carried out.

Condition - 1st Attendance 22/10/40 Copious nasal discharge was present.

Pus Mixed infection; no diphtheroids.

Ionization Following irrigation, ionization with 5% Prontosil was carried out for 4 - 5 minutes at 3½ - 5 M.A.

Treatments given Four.

Result One treatment resulted in a thin discharge only being present. After three treatments there was no discharge, but a further treatment was nevertheless given.

Follow-up 10/11/41 "I have remained free from catarrh for 12 months" wrote this woman.

Case No. 16.

Name Mr. L. Age 55 Occupation Works Manager.

History of Lesion In January, 1940 a sudden intense catarrh of his nose developed. X-ray showed dullness of both antra.

Previous Treatment Antral washouts. Atomiser using ephedrine, flavine etc. calcium injections, Vitamin 'D', all had been tried as well as vaccines. He was sent for zinc ionization.

Condition - 1st Attendance. 1/11/40 Yellow, pus-like catarrhal discharge in both nostrils.

Pus Mixed infection.

Ionization One nostril was treated with 5% Prontosil at 3½ M.A. for five minutes. The other nostril was treated with Zinc.

Result Prontosil gave the greater relief, the discharge was considerably reduced. Zinc showed some, but not so marked an improvement. He refused further Prontosil treatment as it disfigured his lip and stained his handkerchiefs!

Remarks Even the patient agreed that the Prontosil ionization was the better of the two. This was

definitely not psychological, as the opposite opinion would have been expected. Nothing definite can further be deduced from this case except that Prontosil had resulted in a little improvement. It may be mentioned that the zinc treatment did not cure his condition in the end.

Case No. 17.

Name T.O.H. Age 19 Occupation Engineer.

History of Lesion February 1937 - Otitis Media with mastoid abscess 10 days later.

Previous treatment mastoid operation 8/7/37. Healed by 18/9/37

12/10/37 Pus oozed from the old mastoid incision.

14/7/38 Sulphanilamide was tried per Os and again on 27/2/39

4/11/40 Mastoid operation again performed.

Condition - 1st Attendance. 7/11/40 The Incision was not fully closed, so after routine irrigation with diluted Peroxide of Hydrogen, ionization was given.

Pus Staphylococci, streptococci and pneumococci.

Ionization 5% Prontosil at 3 M.A. for 4 minutes was used.

Result One treatment made the patient comfortable, de-odorised the wound. The pus became thin and the wound healed after two treatments. A week later, watery pus oozed from the ear. Nineteen further treatments were unsatisfactorily given to the ear - the aperture in the drum was small. On 3/1/41

pus commenced to ooze from the mastoid incision. Treatment was stopped and he underwent a further operation.

Treatments given Twenty-two

Follow-up On 11/8/1941 pus again began to issue from the ear and from the mastoid area through the operation scar. A polypus was now seen to be present behind the drum

Remarks No ionization with Prontosil could cure a polypus.

Name Miss J. Age 53 Occupation Housewife

History of Lesion For several years this patient had recurring attacks of Pharyngitis and Tracheitis. Both Antra were blocked (Xray)

Previous Treatment Medicinal treatment; Antral washouts.

Condition - 1st Attendance. On 2/1 /41 this patient was sent from the theatre after a wash-out.

Pus No swab was taken under the circumstances.

Ionization 5% Prontosil at 4 M.A. for 5 minutes was used.

Result One nostril was perfectly clear the following day, the other did not show very much catarrh.

Follow-up Two weeks later she reported no catarrh worth mentioning and on 8/4/41 reported quite clear.

Remarks. One treatment only was able to be given. This apparently resulted in a cure. As this may have been a catarrh of nervous origin there may have been a psychological effect behind the result. It is regretted that no swab could here be taken.

Case No. 27

Name Shirley D Age 7 Occupation Schoolgirl

History of Lesion For four years she had suffered from constant nasal catarrh, mouth breathing and cough.

Previous Treatment Her tonsils and adnenoids had been removed when three years old and again, two years later. Vaccines, calcium orally and parentally, Ultra Violet Ray treatment (general and by Kromayer lamp locally) had all been tried.

Condition - 1st Attendance. 13/1/41 The turbinals were enlarged and there was much catarrh in both nostrils.

Pus Mixed infection.

Ionization The nose was packed with gauze soaked in 5% Prontosil and a current of 4 - 10 M.A. was passed for 5 - 10 minutes.

Treatments given Five

Result Slight catarrh was present but she breathed better and now slept with her mouth closed. The turbinals were no longer enlarged. Her mother said "If she stays like this, we shall not grumble."

Follow-up June, 1941. This patient was encountered in the street. Her mouth was closed. She had had no catarrh since her last treatment.

Remarks. Cure.

Case No. 48

Name Miss H. Age 25 Occupation Nurse.

History of Lesion Nasal and post-nasal catarrh and headache had troubled this young woman since she was a girl.

Previous Treatment Tonsilectomy was performed in 1925, 1938, 1941 and sub-mucous resection and antral washouts in 1941. Inhalations, sprays and sulphanilamide had been tried.

Condition - 1st Attendance. 30/9/41 Her throat was inflamed, her teeth were good, a thin discharge was present in her nose.

Pus Staphylococcus aureus.

Ionization 2½% Prontosil was used on gauze to pack the nose, and for 10 minutes 3 M.A. were passed.

Treatments Four treatments were given to the nose.

Result The catarrh ceased. The throat was not treated and remained somewhat inflamed but less than before treatment.

Follow-up 14/11/41 No further trouble has occurred in the nose. It has been free from catarrh. The throat was improving too.

Remarks. The part treated was cured and has remained so for two months, after having had daily catarrh for at least 16 years.

Case No. 51

Name Mrs. M. Age 35 Occupation Housewife.

History of Lesion Nasal Catarrh for 10 years was the complaint.

Previous Treatment Tonsillectomy 10 years ago
Double Antral operation 5 years ago
Antral Washout October 1941
Nasal douches inhalations, vaccines

Condition - 1st attendance Mucous catarrh was present. The left nostril showed the mucous membrane to be swollen and inflamed. The turbinals were enlarged.

Pus Staphylococci Aureus and Albus and Diphtheroid bacilli (No K.L.B.)

Ionization 2½% Prontosil was used at 4 M.A. for five minutes. Treatment was given once a week.

Treatments given Two

Result Following the first treatment she was free from catarrh for three days, then slight catarrh followed. After the second treatment she had a very comfortable week with hardly any catarrh at all

Follow-up She is still under treatment.

Case No. 53

Name Miss C. Age 39 Occupation Home duties.

History of Lesion Following sore throats and nasal catarrh seven years ago, tonsillectomy was performed but bronchiectasis supervened. The catarrh was not cured. Pain developed in the antral regions a few months ago.

Previous treatment Antral washouts.

Condition - 1st Attendance She attended on 2/12/1941 after an antral irrigation.

X-ray This showed dullness of both antra, hence the operation.

Pus Mixed infection

Ionization 2½% Prontosil was used at 3 M.A. for three minutes.

Treatments given Two 5/12/1941

Result Some improvement but, of course, it is too early to claim this as definite.

Follow-up She is still under treatment.

Case No. 8

Name Mrs. S. Age 42 Occupation Housewife

History of Lesion 1938 Phelgmasia Alba Dolens

Three large Varicose Ulcers developed

Previous Treatment Many elastoplast bandages

19 Kromayer Lamp treatments

Various ointments including sulphanilamide.

Condition - 1st Attendance 12/8/40. Three deep varicose ulcers were present on one leg, no corium was present. Two of the ulcers measured 2 square inches and one, one square inch in area. Pus half filled these craters.

Pus -

Ionization 2½% Prontosil at 10 M.A. for 15 minutes was given weekly.

Result After nine treatments, the ulcers were clean, granulations were showing and the area had been reduced by one third.

Slow progress was kept up and by 5/1/1941 the smaller ulcer had healed. One of the large ulcers was the size of a pea, the other was less than half the original area, and level with the normal skin.

Healing slowed down and treatment was stopped on 3/1/1941. She returned on 17/1/1941 as the ulcers had grown rapidly and pus seeped through the bandages. Treatment was redommenced

Treatments given Twenty

Follow-up October 1941. The ulcers had been healed for three or four months.

Remarks. There was no dramatic healing. In this particular case, compared with the long trials by other methods over two years, ionization was effective and soothing. When the treatment was stopped the ulcers very quickly broke down.

Case No. 18

Name Raymond H. Age 7 Occupation Schoolboy

History of Lesion This boy had a severe impetigo contagiosa and for five months had been treated at the Child Welfare Clinic.

Previous Treatment Elastoplast strips and ointments had been used. He was given General Ultra Violet Ray treatment as asked for.

Condition - 1st Attendance. 21/10/40 Two ulcerated areas, one 2" in diameter, the other $1\frac{1}{2}$" x $\frac{1}{2}$": would not heal. Prontosil ionization was used.

Pus Staphylococci Aureus

Ionization $2\frac{1}{2}$% Prontosil at 4 M.A. for five minutes was used.

Treatments given Three

Result After one treatment, the ulcers had nearly healed, but were scratched to pieces after the second treatment. Two further treatments resulted in a good healthy skin.

Follow up 24/2/41 Fit and healthy, no blemishes on skin.

Remarks. The skin cases so far considered would indicate that, when ulcers are not denuded of the entire skin, Prontosil ionization stimulates growth, and kills infection very quickly.

Case No. 25

Name Mrs. W. Age 47 Occupation Housewife.

History of Lesion Mrs. W. had a varicose ulcer on her right leg, for 10 years.

Previous Treatment She had had many veins injected and for many months on end wore Elastoplast bandages. Ointments and vitamin injections were all tried.

Condition - 1st Attendance 8/1/41 A deep, corium-less indolent ulcer 3" x 4" was present on her right leg.

Wassermann Reaction Negative.

Ionization Ionization with 5% Prontosil at 5 M.A. for 6 - 10 minutes was given, twice weekly.

Result Four treatments were required before the base looked healthy. Improvement was gradual. By 28/2/41 the ulcer measured 1½" x 2", after 10 treatments had been given. A further 15 treatments resulted in a reduction in size to a quarter of the original. 12/8/41. After two weeks rest her ulcer was still quiet, almost level with skin, but lifeless in appearance. Slow growth followed.

Treatments given Twenty five.

Follow-up This patient was seen in November 1941. A small

crater the size of a lentil was all that remained unhealed and this was dry.

Remarks The progress in this case resembles the preceding one, slow to start up from rest, gained a fairly rapid movement, then the motive power seemed to become tired and growth became almost stationary.

Case No. 26

Name Mr. F. Age 23 . Occupation Engineer.

History of Lesion For 5 years this man had varicose ulcers on his legs.

Previous Treatment Some veins had been injected, part of the Femoral vein had been excised, injections of arsenic, ointments including sulphanilamide, Elastoplast bandage and Ultra-violet Ray treatment had all been tried.

Condition - 1st attendance. On 16/1/41 there was present on the left leg an ulcer the size of half-a-crown and on the right leg one the size of a florin were present. The W.R. was negative.

Ionization 5% Prontosil at 5 M.A. for 10 minutes was used.

Treatments given Five.

Result Both ulcers were healed except for a minute area, the size of a pin-head on one ulcer.

Follow-up It has not been possible to trace this man. No reply has been received to several enquiries.

Remarks. The growth here was quite dramatic. The ulcers were not entirely devoid of points of granulation tissue. For ulcers, which had been constantly present for five years, to heal in two weeks was more than satisfying 119.

Case No. 29

Name Mrs. W. Age 39 Occupation Housewife.

History of Lesion This woman had onychiae of her finger nails for four years.

Previous Treatment Ointments and lotions had been used; X-ray treatment for six months had been given.

Condition - 1st Attendance. 10/4/41. Her right thumb nail was very badly affected, next in severity her fifth right finger nail and least affected was her left thumb nail.

Pus No fungus was found microscopically and a culture could not be made.

Ionization This case was only undertaken as an experiment. The nails were treated as follows:

	Most affected nail	Badly affected nail	Least affected nail
	2½% Prontosil at 10 M.A. for 15 mins.	1% Copper sulphate at 10 M.A. for 15 mins.	1% Zinc sulphate at 10 M.A. for 15 mins.
Result	Improved after six treatments	greatly improved after six treatments	No change after six treatments

Follow up After one month's rest from treatment, the nail which had been treated with copper was

decidedly better, the Prontosil had not prevented retrogression whilst the nail treated with Zinc was much worse.

Remarks. The action of a sulphonamide on a fungus being unknown this treatment was, as stated, carried out purely as an experiment. The improvement was not marked.

Case No. 32.

Name Mrs. C. Age 36 Occupation Housewife

History of Lesion For at least ten years, her fingers and hands had been raw and bleeding. Her feet too were sometimes affected.

Previous treatment Various ointments

Condition - 1st attendance. All fingers and both hands and scattered areas on both feet were more or less raw, encrusted with pus and dead epithelium.

Pus Mainly staphylococcus aureus.

Ionization The right hand was treated with 2½% Prontosil for 6 - 20 minutes at 6 - 30 M.A.

The left hand (the least affected) was given ultra-violet ray treatment.

The feet were treated with 1% Zinc chloride.

Treatments given Fifteen

Result After nine treatments, the Prontosil had greatly improved the condition, there was no change with the ultra-violet Ray treated hand, the feet had not improved as much as the Prontosil-treated hand. All were changed to Prontosil, six further treatments were given to 20/6/41 when all the sores had healed.

As the skin was very dry Olive Oil and infra-red rays were applied.

Follow up 12/8/41. No sores anywhere could be found but the skin was still very dry.

Case No. 34

Name Mrs. N. Age 55 Occupation Housewife

History of Lesion Hyperkeratosis and ulceration of both hands for over one year.

Previous Treatment X-ray treatment had been given for many months; infra-red ray treatment plus olive oil and ointments of various kinds had been applied.

Condition - 1st Attendance The skin of her fingers was thick, rough and deep raw fissures were present on her knuckles.

Ionization She was sent from the X-ray department with the request "to give her something" during the absence of some of the staff, but not to give her ultra-violet ray treatment.

$2\frac{1}{2}\%$ Prontosil at 5 M.A. for 10 minutes was utilised

Result The raw areas showed no signs of healing after three treatments. The hyperkeratosis was not affected.

Remarks No change in her condition was observed.

Case No. 37

Name Mr. B. Age 27 Occupation Engineer.

History of Lesion A day or two before Christmas 1940, this man's right foot slipped down a manhole, bruising the skin. Dermatitis followed.

Previous treatment Ointments.

Pus Mixed infection

Condition - 1st Attendance 14/5/41 From the ankle to the knee, his whole right leg was covered with a crusted pustular dermatitis.

Ionization He was given treatment for 15 - 20 minutes with 2½% Prontosil at 15-40 M.A.

Treatments given Fourteen.

Result A few treatments showed improvement, then at his next attendance, the leg was as bad as ever. Subsequent treatments resulted in no change for the better.

Remarks. As all previous skin lesions had reacted so well, it was hoped that a similar result would have been obtained. There is no doubt that he scratched some areas which showed a little improvement and also he was determined to have compensation.

Nevertheless, I do not think he destroyed entirely the growth which should have shown if Prontosil was going to have been successful.

Case No. 38

Name Miss P. Age 25 Occupation Household duties

History of Lesion This young woman scratched her fingers whilst cutting roses, a fortnight before attending at the Department. Pustules formed then the pus spread under the epidermis.

Previous treatment Boracic lint dressings; baths in Dettol.

Pus Staphylococcus Aureus.

Condition - 1st Attendance. 22/7/41 The second and third fingers of left hand up to the hand were swollen and entirely denuded of normal skin. Raw shining weeping areas were interspersed with areas of pus, scabs and epithelial debris.

Ionization For 15 minutes, 2½% Prontosil was used at 15 M.A.

Treatments given Three

Result After three treatments, the fingers on 29/7/41 were normal in size, new skin had begun to form except at the knuckles, where it was still a little raw. No further treatments were given. On 8/8/41 the fingers were normal.

Follow up Again seen in September, when her fingers were still normal.

Case No. 45

Name Mr. P. Age 71 Occupation Retired.

History of Lesion For more than a year his left leg had been ulcerated.

Previous treatment Ointments and Elastoplast bandage had been tried.

Condition - 1st attendance. 21/10/41 The lower half of his left leg was practically all eczematous. Several varicose ulcers were present in this area. Two were the size of a florin, one that of a shilling and numerous others which were small but deep.

Pus No germs were found.

Ionization 2½% Prontosil was used at 30 M.A. for 20 minutes.

Treatments given Fourteen

Result cured.

Follow-up No relapse has occurred within the month which has elapsed since his discharge.

Case No. 46

Name Mr. W. Age 72 Occupation Retired

History of Lesion For over two months an ulcer on his great toe had gradually become bigger.

Previous treatment ointments and dressings.

Condition - 1st Attendance After admission to the Wards it was found that he was a diabetic. Although large doses of insulin were given his blood sugar never became satisfactory whilst there was no glycosuria

On 10/9/41 the ulcer was $1\frac{1}{2}$" x $\frac{1}{2}$" and was fairly deep.

Pus Staphylococcus Aureus

X-ray No bony disease

Ionization 10 M.A. for 20 minutes was used, $2\frac{1}{2}\%$ Prontosil being the electrolyte.

Treatments Twenty-eight

Result By 7/11/41 the ulcer was one third the original size and a bridge of healthy skin had grown across the middle of the ulcer. Unfortunately on 18/11/41 he had a severe pain in his ankle, his foot became swollen, gangrene set in and spread to the whole foot. Amputation was carried out but the patient died.

Case No. 47

Name Mr. F. Age 39 Occupation Clerk

History of Lesion An ulcer on his 4th right toe had been present for 11 weeks.

Previous Treatment Ointments, Sulphanilamide internally and externally.

Condition - 1st attendance On the inner side of the 4th right toe an ulcer the size of a shilling and $\frac{1}{8}$" deep was present. Pus filled the ulcer.

Wassermann Reaction Negative.

Blood Sugar This was within normal limits.

Pus Staphylococcus Aureus.

Ionization This was given at 4 M.A. for 20 minutes using $2\frac{1}{2}\%$ Prontosil.

Treatments given Four.

Result No change was secured. His doctor asked if he could be admitted for investigation. Excision of the ulcer was carried out on 12/11/1941. He was sent from the Wards on 1/12/41 for Prontosil ionization. Half of the terminal phalanx had disappeared and the whole toe was now ulcerating.

Follow up He is still under treatment and no appreciable change has yet been observed except that the pus is considerably less.

Case No. 6.

Name Sapper R. Age 28 Occupation Soldier.

History of Lesion This man was accidentally shot through his left hand on 14/7/40. The bullet passed between the second and third metacarpal bones.

Previous Treatment An operation was performed in a military hospital but the wound had discharged pus since its infliction.

Condition - 1st Attendance On 18/8/40 the exit wound on the palm of the hand had been about 1½" in diameter and was now a discharging sinus the size of a threepenny piece and about one inch deep.

Pus Staphylococci and Streptococci

Ionization For 10 minutes the wound was ionised with 2½% at 6 M.A.

Treatments given Four

Result The wound was completely healed after four treatments (He was returned from the military hospital later for correction of limitation of movement).

Follow up 6/11/41 The hand has remained healed since treatment. The fingers have remained stiff.

Remarks A definite and speedy cure, with no relapse.

Case No. 20

Name Sydney B. Age 17 Occupation Apprentice Engineer

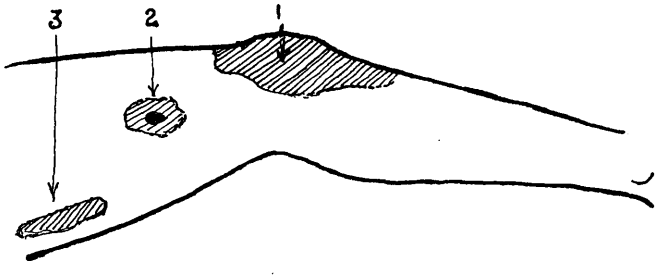
History of Lesion In a car accident on 22/4/40, this young man sustained a compound comminuted fracture of his right Femur.

Previous Treatment An open operation was performed, the fragments of bone being removed and the condyles pinned.

On 13/6/40 he ran a temperature, pus was found under the plaster, which was removed. A large area of his heel, knee and smaller areas were found denuded of skin and were oozing with pus.

Various dressings and sulphanilamide powder were tried. Tersch grafting was carried out on the heel.

Condition - 1st Attendance 4/12/40. The condition of the heel was satisfactory. The unhealed wounds are indicated.



There was no skin over the knee, the wound was filled with pus and measured 6" x 4" (1) Wounds (2) and (3) measured $1\frac{1}{2}$" diameter and 2" x $\frac{1}{2}$" respectively, the former surrounding a sinus $\frac{1}{2}$" in diameter and which squirted pus on pressure.

Pus Short chain streptococci were present.

Ionization 5% Prontosil was used at 4 M.A. for 5 minutes.

Result After 7 treatments wound (1) had healed with the exception of 1 square inch. Wound (2) still oozed pus but only the sinus remained and obviously a sequestrum was involved or the periosteum, although the X-ray report was favourable. The sinus passed down to the bone. Wound (3) was healing but not so dramatically rapid.

After 20 further treatments only the sinus remained unhealed and he was discharged from the wards to attend as an out-patient, 14/2/41.

Lipiadol was injected into the sinus and X-ray showed several winding tracks making their way to the surface at three points as well as to the present opening. Fragments of bone were also observed.

He was discharged on 13/6/41 from the department for operation.

Treatments given Twenty-four

Follow up Operation performed 17/9/41 but this has not yet healed (6/11/41). The pre-patellar wound has never broken down.

Remarks If there had been no sequestra, this boy could have been discharged from hospital after seven treatments. The stimulation of growth of skin was noteworthy, whilst the cleansing action in the inhibition of pus formation was evident after the first treatment.

Ian Kitchin, F.R.C.S. the orthopaedic surgeon, whose patient this was, gave unstinting praise, considering the rapidity with which the skin healed as most surprising.

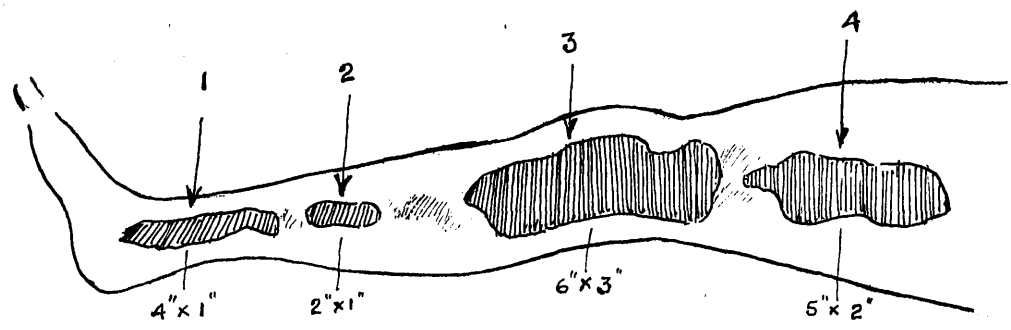
Case No. 22

Name Miss W. Age 58 Occupation House duties

History of Lesion In January 1940, she fell down stairs and fractured both malleoli of her left leg with backward displacement of the astragalus. Wooden splints were used but as sores developed she was sent to the Royal Lancaster Infirmary. The whole leg was very oedematous and large areas were denuded of skin.

Previous Treatment Stimulating dressings, sulphanilamide powder and skin grafts were tried but all failed.

Condition - 1st Attendance 24/12/40. The leg was very wasted, the knee joint and ankle were ankylosed. X-ray showed generalised rarefaction of the bones of the ankle and atrophy of the knee joint. Large raw areas, as indicated were present, the fascia covering the muscles showing when the foul smelling pus was cleared away. The skin between these areas was thin, red, fragile and shiny.



Pus Staphylococci only were found.

Ionization $2\frac{1}{2}\%$ Prontosil was used at 20 M.A. for 10 minutes.

Result After four treatments, there was no smell from the wounds , the patient felt much easier and better, the wounds were clean and dry, granulations were present and there was some growth inwards from the edges.

Fourteen more treatments were carried out. Only one small area, the size of a sixpence, was not quite healed though level with the now normal skin around. This was at the ankle (1). Another, in a like condition but slightly larger was present over the head of the fibula (3). The other wounds were completely healed. She was

discharged after having spent over a year in hospital. On account of the distance from Lancaster she was unable to attend as an out-patient.

Treatments given eighteen

Follow-up 7/11/41 The leg has remained "beautifully healed up"

Remarks The healing here was slower than in the previous case (No. 20). This was to be expected on account of (a) age (b) the longer duration of illness (c) the debilitated state of the patient (d) the larger areas involved. Nevertheless six weeks treatment resulted in a cure after one year of the usual methods of treatment. As in the previous two cases, the new skin was almost normal in appearance, was pliable, thick and in every way satisfactory.

Case 30.

Name Mr. H. Age 18 Occupation Lorry driver.

History of Lesion 3/3/41 His arm was caught in the brake of a heavy trailer and resulted in a T shaped fracture of the humerus and lacerations round the whole elbow.

Previous Treatment Routine dressings and Prontosil powder.

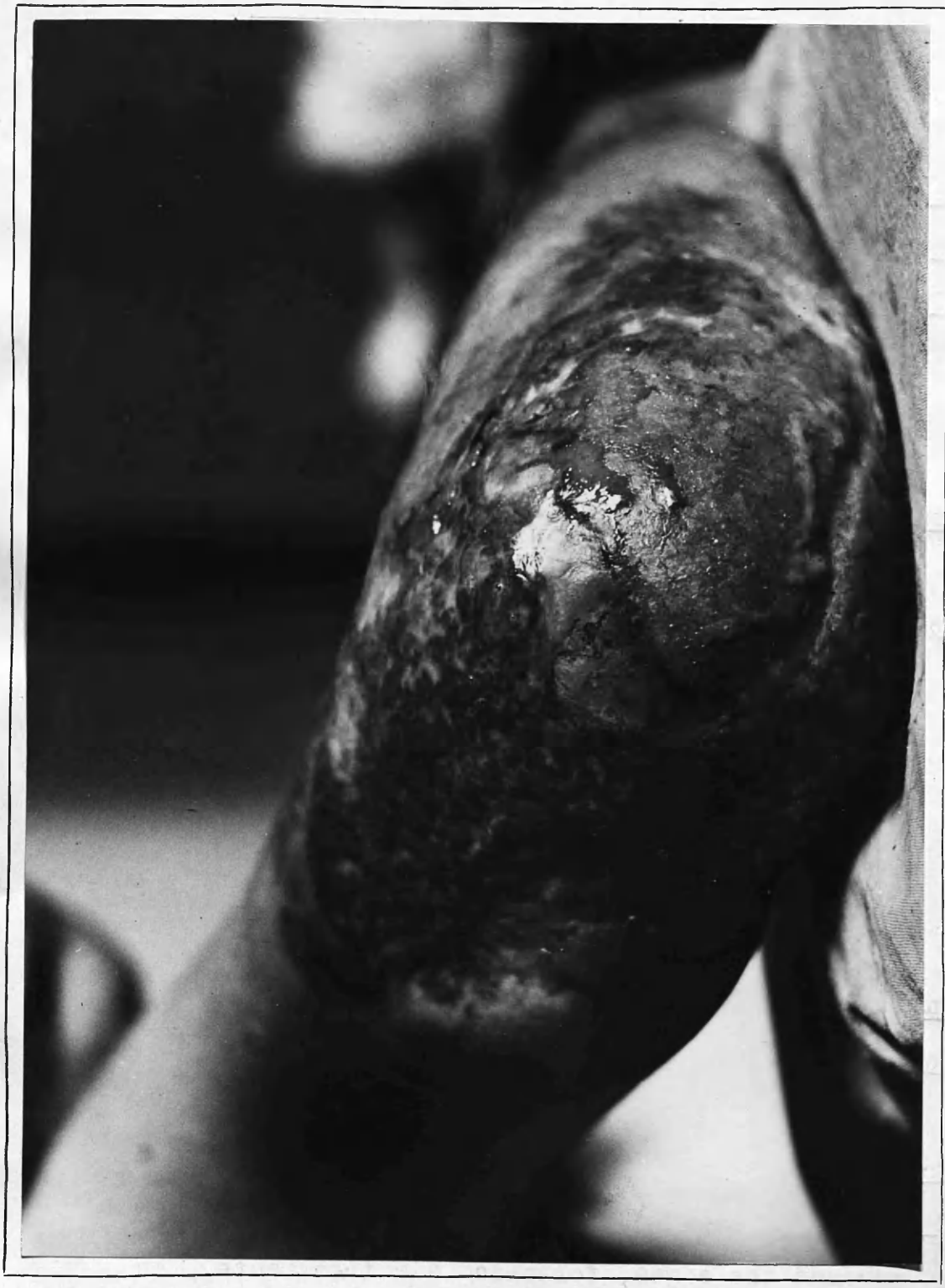
Condition - 1st Attendance 24/4/41 A band 6" wide all round the elbow joint was devoid of skin except for a bridge of devitalised skin 3" wide tapering to 1" in the Anticupital Fossa. Parts of the denuded area were showing fascia or muscle surface and over all, pus was present (See photograph).

Pus mainly staphylococci

Ionization 2½% Prontosil at 10 - 20 M.A. for 10 - 20 minutes was ionised on to elbow, thrice weekly

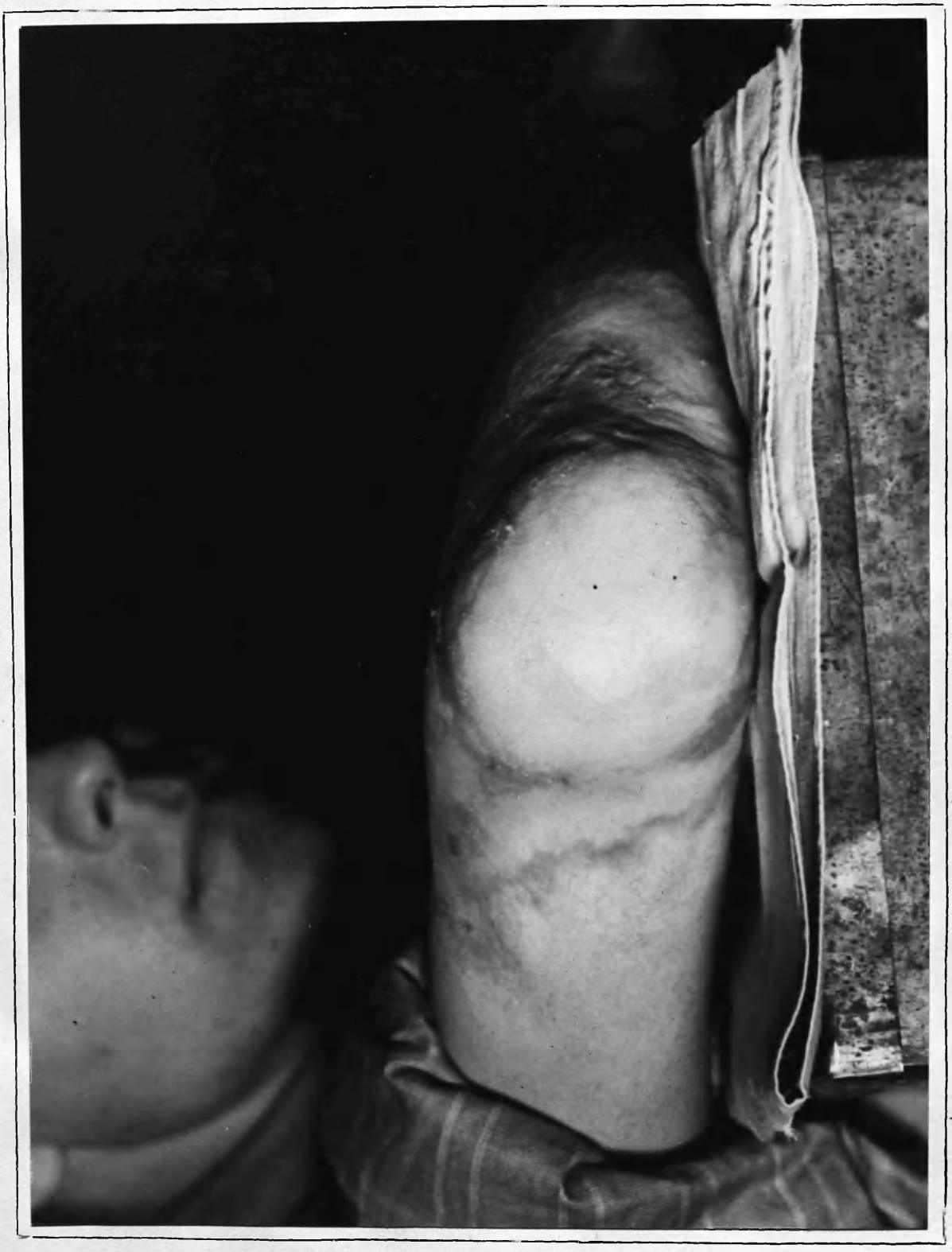
Treatments given eighteen.

Result In two weeks time the skin had grown 1" all round the edges, following six treatments. An additional twelve treatments healed the elbow entirely except for small practically healed points about ¼" in diameter in a line and these



(SEE PAGE 140.)

CASE 30. 24/4/1941. BEFORE TREATMENT.



(SEE PAGE 140)

CASE 30. AFTER TREATMENT, ON DAY OF DISCHARGE 7/6/1941.

were separated from each other by perfectly normal skin. He was discharged on 7/6/41 (See photograph)

Follow up The arm has caused no trouble and remained healed.

Case No. 36

Name Mrs. B. Age 44 Occupation Housewife.

History of Lesion In the first week of May 1941 this woman received a burn on her right foot.

Previous Treatment The foot was first dressed with Genetian-violet but this sloughed. Acriflavine emulsion dressings followed. The foot became septic and oedematous. Vaseline gauze dressings were then used and lastly sulphanilamide powder.

Condition - 1st Attendance. 21/6/41. An area 6" x 4" was denuded of skin. The base of this area was in the main quite healthy but there were only a few small areas indicative of any attempt at growth.

Pus Staphylococci

Ionization For 15-20 minutes 2½% Prontosil was ionised into the wound at 10 M.A. at 3 - 4 days interval.

Treatments given Nine

Result Cured.

Follow-up 29/7/41 The skin over the wound was normal and indistinguishable in quality from the undamaged skin. The scar tissue which was present before treatment with Prontosil was commenced, was raised, thickened, tough like muscle tendons in contraction.

26/8/41 Satisfactory

Case No. 39

Name Mr. C. Age 56 Occupation Travelling crane driver

History of Lesion On 7/7/1941 the crane ran over his right foot severely crushing it.

Previous treatment Following the operation on admission he was treated with Eusol packs, acriflavine dressings and sulphanilamide powder.

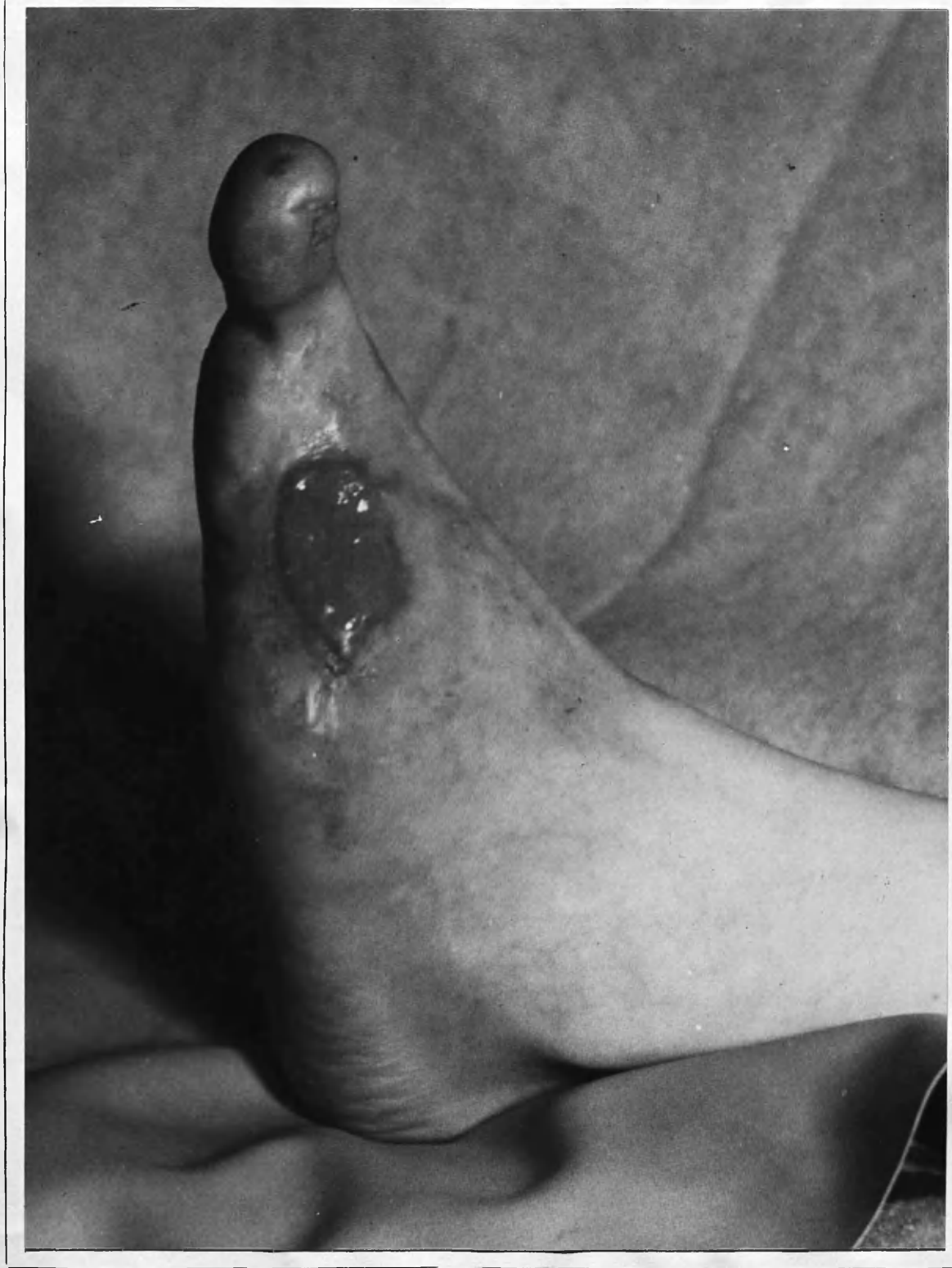
Pus staphylococcu aureus and albus

Condition - 1st Attendance 25/7/41 The photograph on the back of this page shows the condition on this date. With the exception of the great toe, which was slightly injured, all the toes were amputated by the crane. The heads of the metatarsal bones were crushed. Part of the 3rd metatarsal was projecting through the injured muscles. About one third of the foot anteriorly and posteriorly was denuded of skin. This raw area showed as ragged, lacerated muscle and fat, and was covered in most areas with pus. (See photograph.)

Ionization 2½% Prontosil was used for 7 - 20 minutes at 5 - 30 M.A.

Treatments given Fourteen to 25/8/41 when an operation was performed for removal of the protruding bone.

CASE 39. 27/7/1941. BEFORE TREATMENT. (SEE PAGE 142A.)



CASE. 39. 24/9/1941. CONDITION AT TIME OF DISCHARGE FROM HOSPITAL AS AN IN-PATIENT.

Thirty seven to 1/12/41.

Result A thin skin has formed over the whole area with the exception of a part less than a shilling in size at the site where the bone had protruded. The surgeon wished to amputate the great toe and utilise the skin for grafting. The patient would not agree.

Follow-up He is still under treatment (See Photograph).

Case No. 40

Name Alan S. Age 20 Occupation Motor Engineer.

History of Lesion Three days after an injury this young man always bled profusely. He required transfusions in Canada after tonsillectomy and also after a tooth extraction. In 1939 he bled off and on for two weeks after another tooth extraction but this was controlled by a clamp and snake venom injections.

On 29/5/41 he injured the index finger of his right hand. The tip was crushed and the bone splintered. Three days later he started with uncontrollable bleeding and Vit. K. was injected into his left thigh. Two days later his left leg became very swollen overnight. A localised swelling developed over the Tibia when the swelling had receded and then the leg began to swell again. An abscess pointed at the ankle and he was admitted to the Infirmary.

Previous Treatment Vitamin K. Multiple incisions were made in the leg and enormous quantities of pus were released.

Condition - 1st Attendance. 25/7/41 The leg had healed but the finger terminal phalanx was a mass of pulp and pus.

Pus mainly Streptococci (finger)

X-ray Finger - comminuted fracture.
Leg - no bony disease.

Ionization 2½% Prontosil was used for 7 - 20 minutes at 4 - 7 M.A.

Treatments given Fourteen

Result Treatment resulted in complete healing of the finger.

Follow-up 3/10/41 The finger caused no further trouble. It had remained healed.

Case No. 42

Name Mrs. T. Age 57 Occupation Housewife

History of Lesion Mrs. T. sustained a compound fracture of her Right Tibia on 27/10/1938. The leg was in Plaster of Paris for 15 months. The wound never healed.

Previous Treatment Calcium "injections", dressings, including sulphanilamide, had been used.

Condition - 1st Attendance On 5/8/41 there was a raw wound on the lower third of her right leg. This wound was more than skin deep, measured 1" x ½" in area and was anchored to the bone.

X-ray (August 1941). This showed no bony disease.

Wassermann Reaction Negative.

Pus Staphylococcus Aureus.

Ionization 2½% Prontosil for 10 minutes at 20 M.A. was used.

Treatments given Twenty-five.

Result Cured. This patient was extremely slow in responding to treatment - fifteen weeks passing before perfect healing was secured.

Follow-up She was discharged on 25/11/1941, so there has not yet been much time for any possible recrudescence of the ulceration.

Case No.43

Name Mr. W. Age 28 Occupation Cellulose Acetate Worker

History of Lesion On 7/7/39 this man was in a motor cycle accident and sustained a compound fracture of his left tibia. The plate became loose on 27/11/39 and an ulcer formed which had persisted, varying in size but never healing.

Condition - 1st Attendance An indolent ulcer about 1 square inch in area and two small ones about the size of peas, were present over the tibia of his left leg (25/7/41).

Pus Staphylococci

W.R. Negative

Ionization 2½% Prontosil was used at 7 - 20 M.A. for 10 - 15 minutes.

Result The healing had varied. At times it was progressing satisfactorily then the ulcer would be back in its old condition at his next attendance. It finally was perfectly healed by 14/11/41.

Treatments Twenty seven were given.

Follow-up No breakdown had occurred one month later.

D I S C U S S I O N

D I S C U S S I O N

It is now necessary to marshall the facts which will help to give the answers to the questions originally set.

The experiments showed that Prontosil is suitable to act as an electrolyte (Experiment 1 et seq). The rate of introduction of the drug and its depth of penetration are greatly enhanced by ionization as compared with that obtained by osmosis when it is merely applied by directed contact or application (Experiments 1, 2, 4 & 5). In mammalian tissue, ionization carries Prontosil into muscle tissue if applied to a raw surface, and deeply into tissues along blood vessels, being found eventually in the bone marrow itself. It does not ionize through fascia, which dams it up, and along which it flows, but passes into the adjacent muscle via blood vessels (Experiment 10).

The inhibitory action of Prontosil against staphylococcus Aureus was greatly increased when ionization was utilised (Experiments 6, 7, 8 & 9). This is a most important point from a clinical point of view. It is important as it will be equally

efficacious in acute and chronic cases. In the latter, too, the absorption of drug necessary is reduced to a negligible quantity and at the same time the inhibition of growth of bacteria is greatly increased.

The cases treated have been diverse in character, the great majority being chronic cases where other methods had failed. The results secured therefore are more favourable than the percentage cures would at first seem to indicate. Of course it cannot be said that, if the cases had been treated by this method at first, all would have been cured, but it is only reasonable to expect that some of those not cured would have entered this category if treated earlier. Without the diversity of character of the lesions treated, it would have been impossible to gain any idea as to the suitability of cases for treatment in the future. On the other hand this very diversity detracts from impressiveness in results which are so clear cut when one clinical entity alone is reviewed. Nevertheless where numbers are small and no definite conclusions can be deduced, signposts at least give indication of what one may expect in the treatment.

Fifty five cases have been treated and the most

important features breifly set out in the previous notes. Seven cases are still under treatment. Table I gives a summary of the cases under consideration, and these have been tabulated in chronological order. Later tables are added showing the cases collected according to the nature of the lesion, infection involved etc. Cases 12, 29, 31, 34, 41 were given treatment as it did not seem unreasonable that Prontosil Ionization might be effective against the organisms present.

TABLE 1.
SUMMARY OF CASES.

Case No.	Type of Lesion	Organisms isolated	Duration of Disease	Duration of Treatment	Strength of Drug	No. of Treatments	Had sulphanil. previously	Result
1.	Paronychia	-	5 months	1 week	3 %	2	No	+++
2.	Abscess	Mixed	4½ years	10 weeks	3%	20	orally	+++
3.	(Nasal Catarrh (Cellulitis	Staphs.	1 year	7 weeks	3%	11	orally	+++
4.	Otitis Media	Staphs: Streps:	1 year	3 weeks	2½%	6	No	++
5.	Periostitis	Staphs: Streps:	4 weeks	2 weeks	2½%	4	No	+++
6.	Accident W	Staphs: Streps:	5 weeks	2 weeks	2½%	4	No	+++
7.	Otitis Media	Streps:	9 years	2 weeks	2½%	6	No	+++
8.	Varicose Ulcer	-	2 years	20 weeks	2½%	20	No	+++
9.	Carbuncle	Mixed	1 week	1 week	5%	3	No	+++
10.	Periostitis	Mixed	9 months	4 weeks	2½%	21	orally	+++
11.	Otitis Media	Staphs: Streps:	5-6 years	8 weeks	2½%	14	No	+++
12.	Nasal Dip.	Diphtheria	4 months	7 weeks	2½%	10	orally	+++
13.	Nasal Catarrh	Streps: Staphs:	4 years	5 weeks	5%	10	orally	-
14.	Periostitis	Mixed	6 months	1 week	2½%	2	No	+++
15.	Nasal Catarrh	Mixed	many years	3 weeks	5%	4	No	+++
16.	Nasal Catarrh	Mixed	10 months	-	5%	1	No	(++)
17.	Otitis Media	Mixed	3 years	8 weeks	5%	22	orally	-
18.	Impetigo	Staphylococci	5 months	2 weeks	2½%	3	No	+++
19.	Periostitis	Mixed	6 months	4 weeks	5%	10	No	+++
20.	Accident W.	Streptococci	8 months	11 weeks	5%	24	orally	+++
21.	Periostitis	Pneum: Staphs:	5 weeks	6 weeks	5%	15	No.	+++
22.	Accident W.	Staphs:	12 months	9 weeks	2½%	18	Locally	+++
23.	Nasal Catarrh	-	many years	-	5%	1	No	+++
24.	Pilonodal abscess	Streptococci	1½ years	23 weeks	2½%	45	No	+
25.	Varicose Ulcer	-	10 years	15 weeks	5%	25	No	++
26.	Varicose Ulcer	-	5 years	2 weeks	5%	5	No	+++
27.	Nasal Catarrh	Mixed	4 years	4 weeks	5%	5	No	++
28.	Abscess	Streps: Staphs:	2 months	10 weeks	2½	18	No	+++
29.	Onychia	? Fungus	4 years	3 weeks	2½%	6	No	-
30.	Accident W.	Staphs:	7 weeks	6 weeks	2½%	18	Locally	+++
31.	Adenitis	T.B.	1 year	1 week	2½%	1	No	+++
32	Dermatitis	Staphs:	10 years	6 weeks	2½%	15	orally	++
33.	Abscess	None found	7 months	16 weeks	2½%	44	No	+++

TABLE 1 (continued)

Case No.	Type of Lesion	Organisms isolated	Duration of Disease	Duration of Treatment	Strength of Drug	No. of Treatments	Had sulphanil. previously	Result
34	Dermatitis	-	1 year	1 week	2½%	3	No	-
35	(Abscess (Gangrene-skin	Mixed	9 months	2 weeks	2½%	4	No	+
36	Burn	Staphylococci	7 weeks	3 weeks	2½%	9	No	+++
37	Dermatitis	Mixed	20 weeks	6 weeks	2½%	14	No	-
38	Dermatitis	Staphylococci	2 weeks	1 week	2½%	3	No	+++
39 T	Accident W.	Staphylococci	3 weeks	18 weeks	2½%	51	orally	++
40	Accident W.	Streptococci	4 weeks	5 weeks	2½%	14	orally	+++
41	Periostitis	T.B.	8 months	1 week	2½%	1	No	-
42	Accident W.	Staphyococci	3 years	14 weeks	2½%	25	locally	+++
43	Accident W.	Staphylococci	2 years	11 weeks	2½%	27	No	+++
44	Accident W.	Staphylococci	3 weeks	5 weeks	2½%	14	orally) locally)	+++
45	Varicose Ulcer	-	1 year +	5 weeks	2½%	14	No	+++
46	Ulcer	Staphylococci	9 weeks	10 weeks	2½%	28	No	+
47	Ulcer	Staphylococci	11 weeks	2 weeks	2½%	4	Orally) locally)	-
48	Nasal Catarrh	Staphylococci	15 years	2 weeks	2½%	4	Orally	+++
49 T	Ulcer	Mixed	36 years	4 weeks	2½%	12	No	++
50	Abscess	Mixed	13 months	2 weeks	2½%	5	No	+
51 T	Catarrh	Mixed	10 years	2 weeks	2½%	2	No	++
52 T	Accident W.	Staphylococci	5 weeks	4 weeks	2½%	9	No	++
53 T	Catarrh	Mixed	7 years	1 week	2½%	2	No	
54 T	Wound	Staphylococci	5 months	1 week	2½%	2	No	
	←(External) Abscess	Streptococci	4 years	5 months	2½%	41	No	+++

Key Accident W = Accident Wound. Staphs = Staphylococci. Streps = Streptococci. Pneum. = Pneumococci
+++ = cure. ++ = greatly improved, + = improved - = No change. T = Patient is still under treatment.

The results obtained are summarised in the following table. Two cases under treatment are not included.

TABLE 2

Summary of Results

No. of cases	Cured	Greatly improved	Improved	No change	Worse
53	33(62%)	9 (17%)	4 (8%)	6 (11%)	1 (2%)

At the commencement of this investigation, and when 5% Prontosil was unobtainable, a weak solution was used. No harm to tissues was observed; no pain was experienced due to the strength of the solution. At the commencement of treatment all patients, without exception, stated they felt more comfortable, and it was only in late stages, when wounds were healing, that some said the treatment was painful and gave a sensation of drawing. Reduction in the strength of the current used relieved the pain. 58% of patients were cured when 5% Prontosil was used against 63% cured with less than 5% Prontosil (Table 3). These figures are fairly close.

TABLE 3

Comparison of Results

with

Different Strengths of Prontosil

Prontosil	No. of Cases treated	Cured	Greatly improved	Improved	No change
5%	12	7 (58%)	3 (25%)	-	2 (17%)
Under 5%	41	26(63%)	6 (15%)	4 (10%)	5 (12%)

There would appear to be no benefit therefore in using a very strong solution. 2½% appears to be a useful strength to use.

TABLE 4

Treatment required for Cases Cured

or Greatly Improved.

Average Duration of Disease	Average Duration of Disease	Average Number of Treatments.	
175 weeks	6 weeks	13	

Table 4 shows the average duration of all the diseases was 175 weeks, 6 weeks was the average duration of treatment, and the average number of treatments given was 13. Some of the cases had been sufferers for five or ten years or more and this would certainly make these figures more impressive. Neglecting cases over one year's duration, the average duration of disease was 37 weeks, 5 weeks was the average duration of treatment and the average number of treatments given was 12. Again, cases showing no change had an average duration of disease of 98 weeks. The average number of treatments given was 9, spread over 4 weeks. In brief, four weeks treatment will show much improvement or cure or no change at all. Fortunately 79% were in the former category.

T A B L E 5.

Results secured against different organisms.

Organisms	No. of Cases treated	Cured	Greatly improved	Improved	No Change
Staphylococci	14	10 (71%)	3 (22%)	1 (7%)	-
Streptococci	5	4 (80%)	-	1 (20%)	-
Staphylococci & Streptococci	6	4 (66%)	1 (17%)	-	1 (17%)
Mixed	15	7 (47%)	4 (27%)	2 (13%)	2 (13%)
Tubercle b.	2	1	-	-	1
Diphtheria	1	1	-	-	-
Fungus	1	-	-	-	1

The cases have been separated into categories according to the organism involved and this is summarised in Table 5. The fact that the Diphtheritic case (12) was cured shows a possible use for this method of treatment in refactory cases of nasal diphtheria. Conversely it cannot be said that the method is of no use against fungus since the case treated showed no improvement (Case 29). The tubercular cases both resulted in the pus becoming thin and discharging freely after treatment. This fact might account for the case of adenitis being cured after one treatment (Case 31). The hip joint case (41) was definitely ready for a flare up and the treatment acted as detonator. The ionization softened the pus, set free toxins resulting in the pyrexia. The only deduction to be drawn from the above mentioned cases is that it would be of interest to treat further cases.

Lesions infected by streptococci alone are more susceptible to ionization with Prontosil than staphylococci - 80% of the former were cured as compared with 71% of the latter type of case -. The remainder in both infections all showed some degree of improvement (Table 5).

Buttle (40) found that sulphanilamide had only a very slight effect against staphylococci and a very good and rapid effect against streptococci.

Bohlman (32) on the other hand, found that 66% of his streptococcal cases were cured and 6% improved. In the staphylococcal infections 48% were freed from the germs and 20% had reduced growth.

Jensen (36) found sulphanilamide effective against staphylococci.

The general view is that staphylococci are somewhat resistant to sulphanilamide; sulphathiozole and sulphapyridine being more effective. My results may be due to the strain of the staphylococci, or it may be due to the effect of the ionization. The number of cases is not large, but some confirmation that the results secured against streptococci and staphylococci individually are reasonable figures is found in Table 6

T A B L E 6

Results secured against all cases infected by Staphylococci, Streptococci and other germs in combination

Total No. of Cases.	Cured	Greatly improved	Improved	No change
40	25(62%)	8(20%)	4(10%)	3(8%)

Here forty cases infected by these two germs separately, in combination together or in combination with other germs are analysed. 62% were cured and 30% showed some degree of improvement.

Of the three cases which showed no improvement whatsoever, one was a nasal catarrh of four years duration (Case 13), another an Otitis Media of three years duration (Case 17), the other a dermatitis of five months duration (Case 37)

Sixteen cases had received local or oral treatment with sulphanilamide before having ionization. This previous treatment had failed to give any benefit. Of the sixteen cases, eleven were cured, two were greatly improved andthe remaining three showed no change (Table 7).

T A B L E 7

Results of Ionization with Prontosil on Cases previously treated with sulphanilamide.

No. of Cases	Cured	Greatly improved	No change
16	11(69%)	2(12%)	3(19%)

As time passed, it became obvious that certain cases were more likely to benefit from treatment than others, and this apart from the physical well being of the patient. The germs concerned in the lesions were those susceptible to Prontosil (the experimental cases of Diphtheria, Tubercle and Fungus are now ignored). The result seemed to depend on the site and the nature of the surrounding parts. Thus a case of nasal catarrh was given treatment with hopes of a cure whereas a mastoid, possibly due to the anatomical confirmation, was placed on treatment with small anticipated prospect of clearing it up. Again, a traumatic wound was ever so much more likely to heal than a varicose ulcer. To elucidate this point, which is one of those set to answer, all the cases have been arranged in groups, summarised and tabulated in the following tables.

Cases of abscesses are shown in Table 8. Of these 20 cases, 13 (65%) were cured, 2(10%) were greatly improved and 3(15%) showed no improvement at all. The average duration of the disease in those cured was 50 weeks and 13 treatments were the average number required, that is, about five weeks was the time taken. This can surely be considered a very satisfactory result, and be it remarked

once more, especially so in chronic cases where other treatments had been tried and failed. The acute case No. 9, included in the table does not affect the statistics.

TABLE 8

Abscesses = Results of Treatment

Case No	Lesion	Duration of Disease	Treatments given	Results			
				Cured	Greatly Improved	Improved	No change
1	Paronychia	5 months	2	+++			
2	Arm	4½ years	20	+++			
5	Periostitis	4 weeks	4	+++			
9	Carbuncle	1 week	3	+++			
10	Periostitis	9 months	12	+++			
14	Periostitis	6 months	2	+++			
19	Periostitis	6 months	10	+++			
21	Periostitis	5 weeks	15	+++			
24	Pilonodal	1½ years	45			+	•
28	Operation	2 months	18	+++			
31	Neck	1 year	1	+++			
33	Back	7 months	44	+++			
35	Back	9 months	4			+	
41	Periostitis	8 months	1				-
44	Hand	1 month	14	+++			
49T	Periostitis	36 years	12		++		
50	Foot	2 months	5				-
52T	Fingers	5 weeks	9		++		
54T	Operation	4 weeks	1				-
←	(External) -Arm	4 years	41	+++			

T = Still under treatment.

The cases have been briefly discussed in the remarks in the case reports. Where there was free accessibility, the result was pleasing. In the normal course of events expectant treatment would, with some of the periostitis patients, have resulted in a long period of suppuration, quietening down and then further relapses. Many months have passed and no case discharged as cured has reported back with a recurrence. It may reasonably be asserted that abscesses are suitable lesions for treatment by this method. The case, successfuly treated by Mr. Woods, F.R.C.S. and reported in the Section on cases is confirmation of this view.

TABLE 9

Ears and Noses - Results of Treatment

Case No.	Lesion	Duration of Disease	Treatments given	Results			
				Cured	Greatly improved	Improved	No change
3	N. Catarrh	1 year	11	+++			
4	Otitis Media	1 year	6		++		
7	Otitis Media	9 years	6		++		
11	Otitis Media	5-6 years	14	+++			
12	N. Diphtheria	4 months	10	+++			
13	N. Catarrh	4 years	10				-
15	N. Catarrh	many years	4	+++			
16	N. Catarrh	10 months	1		++		
17	Otitis Media	3 years	22				-
23	N. Catarrh	many years	1	+++			
27	N. Catarrh	4 years	5		++		
48	N. Catarrh	16 years	4	+++			
51T	N. Catarrh	10 years	2		++		
53T	N. Catarrh	7 years	2				-

T = Still under treatment.

Diseases of the ears and nose are summarised in Table 9. Nine cases of nasal catarrh were treated. 45% were cured, 33% were greatly improved, and 22% showed no change. The catarrh had been of long duration (an average of five years) but five treatments only was the average given.

There were four cases of Otitis Media with one cure, two greatly improved and one showed no change - 25%, 50% and 25% respectively. The average duration of the disease was 234 weeks and the number of treatments 12. The noses therefore, gave better results than diseases of the ears. This is not due to the germs present, for these were similar to both. The nose is more accessible to cleansing of excessive pus and likewise to more widespread and effective treatment. The ear is difficult of access for cleansing and treatment. The tissues covering the bone in the ear, compared with the nose, must also be taken into consideration in the part played by the defensive mechanism of the body itself. After four years the tissues in the ear are doubtless sodden and inert. A watery solution, such as Prontosil, does not therefore

seem the most ideal vehicle for the presentation of sulphanilamide. All these factors enter into the results obtained. Nevertheless, the cases treated were, once again, all chronic cases. With the more orthodox methods, I believe, about one third of the cases are cured, one third improved and the remaining third no change. If even one, out of every three of the less fortunate patients can be cured and a third more receive further relief, ionization would certainly be worth the time, labour and material involved.

There is no doubt in my mind that Prontosil is greatly superior to zinc in nose and ear cases when pus is present. On the other hand, where no streptococci or staphylococci are present, zinc ionization, I feel, is preferable. True, I have not used Prontosil in any case of Hay Fever and I do not think it would serve any useful purpose when the zinc method is so beneficial, if not entirely specific. This statement is based on past experience. An attempt was made with one patient to treat one nasal passage with Zinc and

the other with Prontosil, in order to compare under identical conditions, the effectiveness of the two electrolytes (Case 16). The patient unfortunately, refused to co-operate.

The results, too, have proved that it is not due to general stimulation of the tissues alone. The electrolyte employed has a definite effect. Again, some of the cases were unaffected by local application of Prontosil, or by oral administration of sulphanilamide, and yet received benefit by ionization. I came across the following quotation which bears on this point - "Sir Almroth Wright and his followers have clearly demonstrated one thing..... that experiments in salt or similar solution..... do not spell finality as far as the germicidal values of various chemical disinfectants are concerned."

As the germs in noses and ears are generally mixed, it might prove more effective to use a mixed electrolyte - Prontosil mixed with sulphapyridine or sulphathiozole, according to the nature of the germ. This would entail an investigation on its own. It might likewise prove useful when given orally.

Mr. A.J. Stout, F.R.C.S., who passed on these cases, summarized his views on the results of ionization as being

'definitely better than local application and certainly useful, though not spectacular.' And with this I agree.

TABLE 10
Diseases of the Skin - Results of Treatment

Case No	Lesion	Duration of disease	Treatments given	Results			
				Cured	Greatly improved	Improved	No change
8	Varicose Ulcer	2 years	20	+++			
18	Impetigo	5 months	3	+++			
25	Varicose Ulcer	10 years	25		++		
26	Varicose Ulcer	5 years	5	+++			
29	Fungus-Nails	4 years	6				-
32	Dermatitis	10 years	15		++		
34	Dermatitis	1 year	3				-
37	Dermatitis	20 weeks	14				-
38	Dermatitis	2 weeks	3				-
45	Varicose Ulcer	1 year	14	+++			
46	Diabetic Ulcer	2 months	28			+	
47	Ulcer	11 weeks	4				-

Four cases of varicose ulcers have been treated and of these, three were cured after having been in existence for one, two and five years respectively (Table 10).

Case 8 broke down rapidly before it was completely healed, when treatment was stopped to see what the result would be. In all cases, there is an initial inertia to be overcome. A rapid clearing of pus follows, and the base becomes healthy. The hope of a subsequent rapid healing is dashed to the ground, as the growth of epithelial tissue fails to follow at the same rate. The surrounding skin appears devitalised for too great a distance around. It does seem, that when the base becomes so clean and healthy, perhaps surgical stimulation or removal of the edges might assist in a more rapid amelioration of the deadlock. In any case, the patients do feel more comfortable. Such being the case, the patients may be on their feet more than they were previously and thus retard healing.

For a severe case of Impetigo, the method might be useful. The skin around is healthy and the treatments required in one case (18) were few and active

healing took place from the commencement of treatment. On the other hand the cases of dermatitis failed to respond - devitalised tissues again. There was no indication, at any time, of a successful or rapid change whatsoever. In brief, for varicose ulcers, ionization is worth a trial; for skin diseases, such as impetigo, pyodermia, furunculosis etc., where the surrounding skin is healthy, the prospects of treatment should be good, but in dermatitis, no.

T A B L E 11

Accident Wounds - Results of treatment

Case No.	Lesion	Duration of Disease	Treatments given	Results			
				Cured	greatly improved	Improved	No Change
6	Hand	5 weeks	4	+++			
20	Knee	8 months	24	+++			
22	Leg	12 months	18	+++			
30	Elbow	7 weeks	18	+++			
36	Burn	7 weeks	9	+++			
39T	Foot	3 weeks	51		++		
40	Finger	4 weeks	14	+++			
42	Leg	3 years	25	+++			
43	Leg	2 years	27	+++			

T = Still under treatment.

Injuries and traumatic loss of skin have shown the most hopeful prospects of all. The results have been dramatic in some and very satisfactory in all Eight patients have been entirely cured and the ninth is now at the stage of being almost cured and ready for discharge. The average duration of the wound before being given ionization treatment was forty-one weeks. The average number of treatments required has been twenty-one.

The bullet wound in Case 6 was completely healed after four treatments. This soldier reported that the M.O. said 'if they can cure a wound like that so quickly , away you go and get them to loosen the stiffness,' and he was sent on leave again. The rapidity of response to ionization was gratifyingly unexpected.

Case 20 had 24 treatments, but it must be noted that the area (for which a skin graft operation was being considered) had been covered over with strong healthy skin after seven ionizations. The other denuded areas had likewise almost healed and only the sinuses remained. These were later proved to be due to sequestra , so that the treatment had fulfilled as much as could be expected of it and saved a skin graft.

The knee had been devoid of skin for eight months and was cured in three weeks. The rapidity of cure induced the orthopaedic surgeon to pass on Case 22.

Case 22 had occupied a bed in hospital for a year and large skin graft operations would have been required. She was sent for treatment with the expectation that she would not react at all. In ten days (four treatments) the sister remarked how pleasant it was to dress the leg now, after the foul odour for so many months. This patient was cured in six weeks.

About 45 square inches of skin had been torn off the elbow in Case 30. By treatment this was replaced in six weeks time. He was a good fit, healthy specimen of virile manhood, and no doubt this was an important point, in the rapidity of cure. When the skin began to grow, it was noticeable from day to day, how rapid this progress was. A skin graft operation was here too avoided.

Case 36 grew a supple skin instead of the tough fibrous, unpliable skin which had formed during previous treatment of a burn on the foot. The growth was not so spectacular as in the previous cases, but was, nevertheless, pleasingly rapid, with a more healthy normal skin than

that usually left after a burn.

These cases have been mentioned as being representative of their type. They were the most successful of all lesions treated. The general concensus of opinion is that it is useless to apply sulphanilamide locally when pus in fair amounts is present. When these wounds had been gently swabbed with Peroxide of Hydrogen and ionized with Prontodil the large amount of pus, which previously formed daily, grew less and less following each treatment. Sloughs too were overcome. As previously stated I believe this to be due to the encircling movement which the ionizing current carries out and the subsequent deposition of the Prontosil. The rapidity of growth of the skin in some of these cases had to be seen to be believed. The result was aesthetically all that could be asked for. The new skin to touch was practically indistinguishable from the surrounding normal skin. Several patients had been treated locally with sulphanilamide powder with no beneficial results. Mr. Ian Kitchin F.R.C.S. who gave me the cases to treat was "surprised at the results, especially as ordinary local treatment with sulphanilamide had been of no use. The healing had been most satisfactory and extraordinarily rapid. It had saved skin grafts."

The results of Prontosil Ionization of traumatic wounds, especially those involving loss of large areas of skin, may be summarised as follows:-

1. It is soothing in effect and increases the comfort of the patient.
2. It deodorises and sterilses the wound.
3. It stimulates rapid growth of epithelial tissue.
4. Skin graft operations may be avoided.
5. Strong, healthy, pliable skin results with no disfigurement.

In my opinion, this method of treatment is the treatment of election in such cases.

SUMMARY

S U M M A R Y

A new method of treating local lesions infected mainly by streptococci and staphylococci has been discussed. It consists of using Prontosil Soluble as an electrolyte and by means of a constant current of a few mille-amperes ionising it into the affected part. Oral administration is avoided. The Prontosil is driven into the tissues and a deeper interaction with the body fluids secured than can be effected by local application alone.

The principle of using a specific drug as an electrolyte against specific germs is also new. A sulphanilamide preparation (Prontosil Soluble) has here been used against streptococci and staphylococci. Sulphathiazole might prove more effective against staphylococci and a mixture of these drugs against a mixed infection. This, of course, requires investigation.

A brief outline of ionization has been given. The history of sulphanilamide is outlined and as complete a record as possible made of the reports in the literature on local application of the drug.

Some experiments have shown the bacteriostatic power of Prontosil Soluble and its enhancement by ionization. The rapidity of penetration and the depth of pentration have proved by experiments to be multiplied very considerably by utilising this method.

During a period of observation of nearly two years, fifty-five cases have been, or still are, under treatment. Practically all were chronic cases where other methods of treatment had failed to alleviate the condition. Chronic cases were sought in this investigation to give the most crucial test possible to the idea involved, the assumption being that acute cases could heal spontaneously. Again, if efficacious in chronic cases, suitable cases could, in future, be selected in their early stages for Prontosil ionization.

Sixteen patients had received sulphanilamide treatment locally or orally without benefit before having ionization. 69% of these were cured and 12% greatly improved.

There was no injury to tissues. The patient was made more comfortable and his feeling of well-being improved. The wounds were de-odorised, the multiplication of germs and production of pus stopped, and the growth of tissues was stimulated.

Of all the cases treated, 62% were cured, 17% were greatly improved, 11% showed no change, and one case(or 2%) was worse following treatment.

The average duration of disease was 175 weeks for those cured or almost cured, the duration of treatment 6 weeks and the average number of treatments required to gain this end was thirteen.

Streptococci were more susceptable to the treatment than staphylococci. For cases cured, the figures were 80% and 71% respectively

Abscesses, the average duration of which had been fifty weeks, showed 65% cures in five weeks time as the result of treatment. A further 10% have been greatly improved, are still under treatment and are approaching the stage of complete cure. When an abscess is deep or is not responding to the usual treatment, ionization with Prontosil Soluble offers a method very hopeful of cure.

Cases of nasal catarrh and antral infection responded well to treatment. Five applications on an average cured 45% and greatly relieved a further 33%, the latter being practically catarrh free. These were chronic cases, the patients having suffered for five years on an average.

Prontosil ionization is quite a useful weapon to fight chronic nasal infections when streptococci or staphylococci are present. Only four cases of chronic otitis media were treated and that not very successfully - one was cured, two improved and one showed no change. The difficulty lies in securing universal contact behind the tympanum.

The response of varicose ulcers to Prontosil ionization was very slow and not impressive. All that can be said is that when other methods fail, it is worth trying. It is ineffective in treating dermatitis but in impetigo contagiosa it was quickly efficient. From experience gained, this treatment could be expected to be equally useful in resistant skin diseases of a pustular type.

Traumatic wounds, with large areas denuded of skin and which normally would have required skin grafts healed quickly and satisfactorily under ionization. Where treatment has been completed, all have healed, and the remaining case still undergoing treatment is almost ready for discharge. The results have been aesthetically good. The new skin was strong, pliable and healthy.

It is suggested that, before skin grafting is resorted to, such wounds should be given, as the method of choice, treatment by Prontosil ionization.

I am indebted to Mr. A. J. Stout F.R.C.S. for supplying the ear and nose cases and to Mr. I. Kitchin, F.R.C.S. for the orthopaedic cases which would have required skin grafts and for the other traumatic cases.

INDEX

of

REFERENCES

INDEX OF REFERENCES

1.	Jones, H. Lewis	"Ionic Medication"
2.	Friel A.R.	"Electric Ionization"
3.	Luff A.P.	Lancet 9/12/1905. 1667
4.	Wells, T. Spencer	Medical Times & Gazette Vol. 7. 1853. 84
5.	Edison Thomas A.	Verhandlungen des X Internationalen Medicinische Congresses, Berlin 4-9 Aug. 1890. Dermatolgie und Syphilidographic. 1.
6.	Cleaves, Margaret A.	Medical Record 25th Aug. 1894. 253.
7.	Leduc, Stephané	"Electric Ions and their use in Medicine,"
8.	Jones, H. Lewis	Lancet 28/10/1905. 1236
9.	Doyle A.A.	Transactions of the Australian Medical Congress Oct. 1908. Vol III. 183
10.	Friel A.R.	"Electric Ionization." Personal communications.
11.	Webb, J. Curtis	Lancet. 4/11/1905. 1361
12.	Tayler H.P.	Bristol Medico-Chirurgical Journal Vo. XXVII. 1909. 132
13.	Finzi, N.S.	Proceedings of the Royal Society of Medicine, 1908-9 Vol. 2. p140
14.	Bokenham T.J.	Proceedings of the Royal Society of Medicine 1908-9 Vol. 2. p. 135

15. Riddell, J.R. Glasgow Medical Journal 1912. 1. 118.

16. Taylor, Stopford & MacKenna, R.W. Liverpool Medico-Chirurgical Journal XXXI. 1911. 168

17. Bailey, L.D. B.M.J. 28/6/41. 986.

18. Gelmo. (Stuck-Texas State J. Med. July 1940 225)

19. Eisenberg. (Stuck-Texas State J. Med July 1940. 225)

20. Mietsch & Klarer (Stuck-Texas State J. Med July 1940. 225)

21. Domagk G. (Klin Wschr. 16. 1412 1937 (Stuck-Texas State J. Med. July 1940. 225)

22. Becker Dtsch-Med. Wschr. 1937.7.321 (Bayer)

23. Purdie, A.W. & Fry R.N Lancet 3rd July 1937 18.

24. Sigel Fortschr. Ther.4 1936. 229 (Bayer)

25. Jaeger Dtsch Med. Wschr. 62.1831 1936 (Bayer)

26. Tiling, B Münch. Med. Wschr. 83. 952. 1936 (Bayer)

27. Colebrook & Kenny Lancet 6th June 1936. 1279

28. Buttle, Gray & Stephenson Lancet. 6th June 1936. 1286

29. Long & Bliss. J.AM. Med. Assocn. 2nd Jan 1937. 32.

30. Sinclair J. Canad. Dent. 3. 571. 1937 (Stuck)

31. Merz Schweiz, Med. Wschr. 16 1937 342.

32.	Bohlman	Am.J. Surg. Dec. 1938, 825.
33.	Mellon	Am. J. Surg. 1938. 825 (Bohlman)
34.	Osgood & Brownlee	J. Am. Med. Assocn. 29/1/1938. 349.
35.	Findlay	"Recent Advances in Chemotherapy." 1939
36.	Jensen, Johnsrud & Nelson	Surgery. July 1939 Vol. 6,1.
37	Stuck Maxwell & Monsalvo	Texas State J. Med. July 1940. 225
38.	Fleming, A.	Proced. Royal Soc. Med. Jan. 1940. 127
39.	Fleming, A.	Pharm. Journal 23/11/40 162. 30/11/40. 172.
40.	Buttle, G.A.H.	Lancet. 11/5/1940. 890
41.	Nitti, F.	Presse Médicale 25-29th. Nov. 1939. 1577
42.	Legroux	Presse Médicale 1-4 May 1940. 456.
43	Russell & Falconer	Lancet 27th July 1940. 100
44.	Hawking, F.	B.M.J. 22/2/1941. 263
45.	Glover, P.	Am. J. Ophth. Feb. 1939.180
46.	Bosse & Bosse & Schirp	Fortschr. Ther. 15. 1939. 202 (Bayer)
47	Chandler	Am. J. Dis. Child. 57 May 1939. 1110
48.	Sézary, A.	Presse Médicale 11/10/1939 1408.

49.	Brittain & Latter	B.M.J. 11. 1940. 284.
50	Hodgson & McKee	B.M.J. 11. 1940. 147
51.	Levaditi, Gerrard-Moissonnier, Brechot & Tournay	Bulletin de L'Academie de Medicine 23-30/1/1940. 39
52	Fuller & James	Lancet 16/3/1940. 487
53	Jones, R. Watson	W. London Med. J. Apl-June 1940. 30
54	War Office "Memorandum concerning the use of Sulphonamide Derivatives 3rd July, 1940	
55.	Page, Max.	B.M.J. 9/11/1940. 640
56.	Colebrook, L.	B.M.J. 16/11/1940. 682
57	Handley, S.	B.M.J. 9/11/1940. 641
58	Ogilvie, W.H.	B.M.J. 9/11/40. 642
59	Page, Max.	B.M.J. 30/11/1940. 731
60	King, A.C.	B.M.J. 15/2/1941. 231
61.	Riches, E.W.	B.M.J. 9/11/1940. 642
62	Buxton, St. J.D.	B.M.J. 7/12/1940, 802
63.	Colebrook, L.	B.M.J. 9/11/1940, 641.
64	Milian, M.	Presse Médicale 25-29/11/1939 1577
65	Childrey, J.H.	Arch. Otolaryng 29.1939. 986
66.	Smith, J.A	B.M.J. 22/6/1940 1016
67	Payne, A.M.M. & Auchinleck, G.M.	B.M.J. 1/3/1940 332
68	Mayo, C.W. & Miller, J.M.	Proc. Mayo Clinic 25/9/1940 609

69. Herrell, W.E. & Brown A.E. Proc. Mayo Clinic 25/9/1940. 611

70 Frankland, A.W. B.M.J. 4/1/1941. 33.

71. Fletcher, F.R. B.M.J. 15/2/1941. 242.

72. Bigler, J.A. & Haralambie, J.Q. Am. J. Dis. Child. 1939. 1110.